Journal of the
Indian Medical Association

Vol XVI, No. 3 CALCUTTA December, 1946

# PENICILLIN IN THE TREATMENT OF DIPHTHERIA

## A Preliminary Note

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### Introduction

The discovery of anti-toxin in the treatment of diphtheria is no doubt the greatest advancement in the field of therapeutics and from time to time other drugs such as anti-streptococcal serum and sulphonamides are also used as adjuncts to combat the secondary invaders of the throat and respiratory tract. Such measures have certainly reduced the mortality due to diphtheria to a considerable extent but whether any drug other than anti-toxin can be used for the cure of diphtheria has not yet been thought of.

Diphtheria is essentially a local infection. The organisms thrive at the point of inoculation and a pseudomembrane is produced locally as a result of the inflammatory reactions. This pseudomembrane, if present in the upper respiratory tube, may cause obstruction to respiration leading subsequently to asphyxia and death. This is rather a mechanical effect. The other and the more common and serious effects are due to the liberation of a powerful exotoxin by the organisms from the local lesion. This toxin after it is absorbed into the circulation exerts its deleterious effects on the cardio-vascular, nervous and urinary systems after a few days or weeks. Moreover, faucial diphtheria is often complicated by respiratory troubles caused by secondary organisms, of which bronchopneumonia is often the cause of a fatal termination. The secondary invaders are commonly pyogenic bacteria which are sensitive to sulphonamides and penicillin.

The value of anti-toxin in the treatment of diphtheria lies in its power to neutralize the powerful exotoxin of *C. diphtheriæ* and thereby giving the defensive forces of the body a chance to overcome the organisms which are manufacturing the toxin. Probably the anti-toxin by neutralizing the toxin gives a reasonable time to the defensive mechanism to mobilize the optimum amount of anti-bodies to overcome the organisms.

Theoretically, the treatment of diphtheria may be considered from another angle, *viz.*, destroying the organisms quickly by some drugs and thereby giving the body a chance to neutralize, excrete, or utilize the toxin for the manufacture of active immunity. In severe infections anti-toxin combined with a specific drug having lethal effect on *C. diphtheriæ* will be the most effective treatment.

### Methods of Study

The sensitiveness of *C. diphtheriæ* to penicillin is well-known and whether it can be used as a valuable therapeutic agent against diphtheria is yet a matter for observation. Several cases of diphtheria (27 cases) were treated with penicillin alone in the Medical College Hospitals, Calcutta, under the supervision of the senior author (M.N.D.) to see its effectiveness in clearing out the infection as compared with cases treated with anti-toxin and sulphonamides which were kept as controls. Keeping in mind that penicillin, though lethal to *C. diphtheriæ* has not got any action on the toxin, only early cases were selected for the trial just to minimize the risk. A few moderately severe cases were also included but a very close watch was kept on them to note at the earliest possible time any deterioration of their condition.

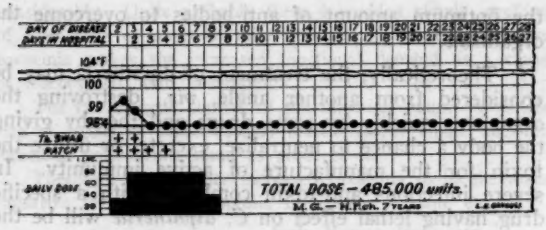
The mode of administration of penicillin in all these cases was 10,000 units intramuscularly every 3 hours with the usual precautions, the first dose being 20 to 30,000 units. Total dosage of penicillin employed was on an average 4,00,000 to 5,00,000 units. The throat swabs were inoculated in the culture tubes before starting the treatment and also daily subsequently. Three consecutive negative swabs were taken as the usual criteria for stopping penicillin. Altogether 27 cases of faucial diphtheria were treated with penicillin alone. All of them were young children, ages varying from 8 months to 11 years. 16 of them were male and 11 female; 24 were Hindus and 3 Muslims.

### Results

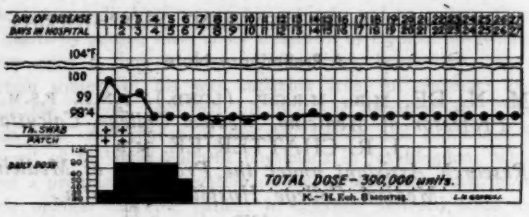
In the majority of them the temperature came to normal level within 24 to 72 hours, small patches disappeared in 24 to 48 hours and extensive ones disappeared within 4 to 5 days. The throat swabs became negative within 1 to 6 days and the general condition improved to a great extent within 1 to 3 days. Though a few cases were admitted with mild respiratory difficulty, they improved quickly and

tracheotomy was not needed in any one of them. None of them had any complications whether cardio-vascular, nervous or urinary. Respiratory complications due to secondary invaders were also singularly absent. All of them recovered and were fit for discharge within 1 to 2 weeks after admission, but as the cardiac and nervous complications of diphtheria do not appear before 2 to 4 weeks, the moderately severe cases were kept for 3 to 4 weeks. In a few cases, the guardians insisted on taking out their children from the hospital 1 week after admission as they thought from the general condition of the patients that they were quite fit. These patients had to be discharged a week after admission but the guardians were earnestly requested to report every week. Most of them did and no fatality has been reported.

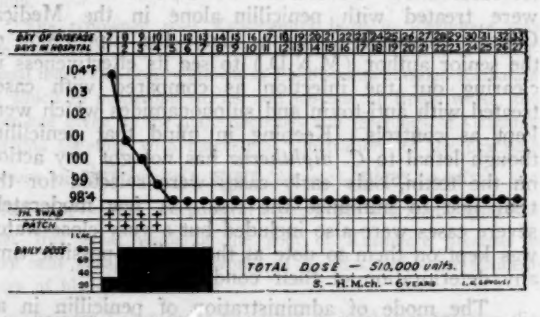
CHARTS OF FOUR OF THE CASES UNDER REVIEW



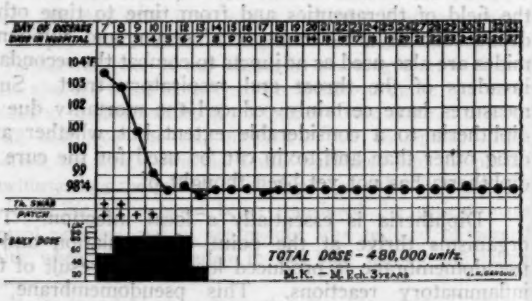

M.G., F.Ch., aged 7 years, was admitted with history of fever, cough, and pain throat for 2 days. Patch both tonsils. Temp.—99·4°F. P/R. 100/22 p.m. Temperature came down to normal on the 3rd day of admission Total dose of Penicillin 485,000 units. Throat swab positive for two days and the patch disappeared on the 5th day. No complications.




K., H.F.Ch., aged 8 months, was admitted with history of fever for 1 day with excessive salivation and refusal of feeds. Temp.—100°F. Patch small on right tonsil only. Total Penicillin 390,000 units. Patch disappeared on 3rd day. Throat swab negative on 3rd day. No complications.




S., H.M.Ch., aged 6 years, was admitted with history of fever, cough and difficulty in deglutition for 7 days. Temp.—104°F. Moderate sized patch on both tonsils. Total dose of Penicillin 510,000 units. Temperature came down to normal on the 5th day. Patch disappeared on the 5th day and throat swab became negative on the 5th day. No complications.




M.K., M.F.Ch., aged 3 years was admitted with fever, cough, bleeding from nose, enlarged cervical glands for 7 days. Temp. 103·8°F. Patch on both tonsils and uvula. Total dose of penicillin 480,000 units. Temperature normal on the 5th day. Patch disappeared on the 5th day. Throat swab negative on 3rd day. No complications.

## DISCUSSION

It will not be proper to draw any definite conclusion from the results obtained in a small group of 27 cases treated with penicillin alone, as the number was not adequate for statistical conclusion; but it will not be out of place to discuss a few points. The quickness with which the general condition improved, the patches cleared up and the throat swabs became negative can well be compared favourably with the result obtained in the classical treatment of diphtheria with adequate doses of anti-toxin and sulphonamides. Respiratory infections due to secondary organisms were not seen in any of them. Cases admitted with mild respiratory obstruction when treated with anti-toxin and sulphonamides sometimes require tracheotomy due to the spread of the diphtheritic membrane further down. In the present series of cases, tracheotomy was not needed in any of them though a few were admitted with mild respiratory obstruction. Penicillin by its lethal effect on *C. diphtheriæ* stopped any spread of the pseudomembrane downwards and thereby prevented tracheotomy, which is not always without danger. The cardiac and nervous complications which are often the dangerous manifestations of diphtheritic toxæmia were completely absent. The nervous complications of diphtheria require special mention for their peculiarity. They are described as types of peripheral neuritis with occasional degeneration of the nerve cells in the brain-stem and spinal cord. They are usually subdivided into 3 groups (1) local, (2)

specific and (3) general. The local nervous complication in a case of faucial diphtheria is paralysis of the soft palate. It appears within a few days and is supposed to be due to absorption of the toxin liberated in the patches. The toxin travels along the local nerves and damages them. The specific effect is paralysis of accommodation which is difficult to detect in children for lack of co-operation. The general effect is paralysis of nerves coming from the brain stem as well as paralysis of spinal nerves. The specific and general effects are caused by toxin which is first absorbed into the circulation and later on acts on the nerves and their nuclei of origin through blood. They appear late *i.e.*, about 2 to 4 weeks after infection.

These nervous complications of diphtheria are not very common, at least in our country. When they do occur they often bear no relation to the severity of the original lesion. When cases were treated with penicillin alone, there was nothing in the system to neutralize the exotoxin except the defensive forces. Had exotoxin alone been the only factor to produce nervous lesions then one would have found a larger number of cases with nervous complications in the patients treated with penicillin alone than in those treated with anti-toxin and sulphonamides, (at least in the severe cases). But no nervous complications occurred in the present series of cases treated with penicillin alone. It is probable that some additional factors other than the diphtheritic exotoxin are necessary for the production of nervous complications. It may be that individual suceptibility or an inherent weakness of the nervous system is one of the chief factors in the production of the nervous lesions.

In the present series of cases treated with penicillin alone the mortality was nil. During the 5 year period, 1941 to 1945, the mortality of diphtheria in the Medical College Hospitals, Calcutta, varied from 20 to 36 per cent. No definite comparison can be made between the above two figures, as only early and a few moderately severe cases were included in the present series, whereas the mortality of 1941 to 1945 was calculated from all types of cases, early, moderately severe and very severe.

From financial point of view, treatment with penicillin alone compares favourably with treatment with anti-toxin and sulphonamides. Average total dosage of penicillin employed in the present series of cases was 4,00,000 to 5,00,000 units costing about Rs. 7|- to Rs. 8|4|- (Rs. 3|8|- for 2,00,000 units of penicillin), whereas average dosage of anti-toxin employed in similar types of cases is 50,000 to 60,000 units costing about Rs. 35|- to 42|- (Rs. 7|- for 10,000 units of anti-toxin). Of course such reduction is only possible in hospitals where the patients are not to bear the cost of the medical attendants (who are to give injections at 3 hourly intervals).

Diphtheria, being a local infection, one may expect that local application of penicillin in adequate concentration and at frequent intervals would have some effect on the infection, and a better effect if combined with systemic injections. In the present series of cases local application was not resorted to for several reasons. In faucial diphtheria, the lesions are constantly bathed in mucus and saliva and so any drug applied locally is liable to be washed away specially in cases of children who swallow saliva frequently. These patients require frequent feedings, which interfere with any local application and they mostly resent repeated administration of drug into the throat and in the struggle they may get exhausted. For these reasons local application of penicillin was considered to be of doubtful value and was not practised in any of these cases.

The disadvantages of treatment with penicillin are well known, such as difficulty in storage, preparation of fresh solutions and 3-hourly injections. The frequency with which the injections are to be given is not only distressing to the patient but it also requires the services of a doctor or a good nurse at an interval of 3 hours and this is surely not advantageous to the patients from pecuniary point of view. If in future, a suitable preparation which can be effectively injected less frequently or more preferably an effective oral preparation be discovered, then a great landmark in the advancement of treatment with penicillin will be achieved. This will be applicable not only to suitable cases of diphtheria but in many other conditions where the organisms are penicillin-sensitive.

Penicillin is doubtless a valuable adjunct in the treatment of all types of diphtheritic infections treated with anti-toxin, but the conclusion as to whether penicillin alone can be used as a valuable drug against early and/or selected cases of diphtheria, is left to be judged by further experience.

## Summary

1. 27 cases of diphtheria treated with penicillin alone are reported.

2. All of them recovered without developing complications.

3. Advantages and disadvantages of penicillin in the treatment of diphtheria are discussed.

4. Possibility of future improvement in the treatment of diphtheria with penicillin alone is also discussed.

The writers offer their sincere thanks to Dr. B. P. Tribedi, M.B., D.B. (LOND.), F.N.I., for his ungrudging help in bacteriological examinations and also to the Superintendent, Medical College Hospitals, Calcutta, for kindly allowing them to use the hospital records and for the supply of penicillin required for this investigation.

# SUBACUTE BACTERIAL ENDOCARDITIS WITH TREATMENT OF TWO CASES WITH PENICILLIN

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Lancisi (1707) described the first case of bacterial endocarditis in a man aged 50 who died of intermittent fever of one year's duration, and who on postmortem examination on 26th September, 1706, showed chronic endocarditis of the aortic valve. Morgagni (1769) recorded two cases of which one died of apoplexy and the other of hemiplegia of the right side, the latter on postmortem showed enlarged spleen in addition to endocarditis of the mitral valve. Corvisart (1813) used the word "vegetations". Laennec (1834) observed the association of bacterial endocarditis with previously damaged valves, and Osler (1885) described in detail the clinical picture and observed its association with congenital heart disease.

Heiberg (1872) isolated "streptothrix" from the vegetations. Klebs (1878) demonstrated cocci and "monads", and Harbitz (1899) cultured streptococcus from the blood in 17 out of 30 cases. Blake (1916) reported a case of subacute bacterial endocarditis produced by streptobacillus moniliformis infection. McDermott *et al* (1945) reported a case produced by the same organism. Treatment with penicillin in this case resulted only in the inhibition of the growth of the organisms but not in complete cure of the patient.

Ribbert (1885) produced endocarditis in dogs by injecting staphylococcus aureus in potato emulsion.

Under the auspices of Harmsworth Memorial Research Fund, Bruce Perry (1936) published the results of his extensive investigations on the clinical and pathological aspect and Lloyd-Jones on the production of endocarditis in experimental animals.

Klee and Romer (1935) introduced sulphanilamide in the treatment of bacterial endocarditis with disappointing results but later trials with and without heparin (Paullin and McLaughlin, 1945) resulted in the arrest or cure of some cases.

Flippin *et al* (1942) introduced penicillin in the treatment of subacute bacterial endocarditis. Although the earlier results were unsuccessful (Herrell *et al*, 1944), favourable results have been observed later (Loewe *et al*, 1944).

Seven cases of bacterial endocarditis observed by the senior author are classified as follows:—

| | | |
|---|---|---|
| 1. | Superimposed on congenital heart disease | |
| | (*a*) Pulmonary stenosis .. | 1 |
| | (*b*) Patent ductus arteriosus .. | 1 |
| 2. | Superimposed on mitral stenosis .. | 2 |
| 3. | Endocarditis of the aortic valve .. | 2 |
| 4. | Endocarditis of the aortic valve associated with chronic interstitial nephritis .. .. .. | 1 |
| | TOTAL .. | 7 |

Diagnosis was made clinically in all the cases except one. Positive blood cultures were obtained in 3 cases. Two cases recovered, both with penicillin. Out of five deaths, postmortem was available in two cases.

## CASE REPORTS

Brief notes of the seven cases are given below:—

*Case 1—Subacute bacterial endocarditis superimposed on congenital heart disease (pulmonary stenosis?).* R.M., Hindu, male child, aged 3 years, was admitted on 16-6-45 with a history of fever and palpitation of 4 months' duration. Fifteen days before admission, the mother putting the hand over the child's chest noticed a thrill. The child was active before but not so now. *Physical examination* showed a fairly nourished child, no gross deformity anywhere, no cyanosis, no clubbing of the fingers. Heart showed slight increase in size. A definite systolic thrill was felt at the base, and a harsh systolic murmur was heard all over the precordium, the maximum intensity being in the pulmonary area. Lungs showed occasional rales at bases, and spleen and liver were just palpable below the costal margin. Radiological examination of the heart did not show any definite enlargement. Urine: No albumin and no sugar, microscopically nothing abnormal. Blood: R.B.C. 3·25 million. W.B.C. 8,000. Differential count—Poly. 69, Mono. 10, Lympho. 16 and Eosino. 5 per cent.

A clinical diagnosis of subacute bacterial endocarditis superimposed on congenital heart disease was made.

The child was put first on 20 gr. of sodium salicylate a day for about a week without any effect. Penicillin was started on 26-6-45, 5,000 Oxford units every 4 hours intramuscularly. It was continued daily up to 11-7-45 and the child had 525,000 units of penicillin. He was discharged free from fever on 12-7-45, and remained for two weeks without any symptoms. Two weeks later, (27-7-45) the child was admitted with relapse and was given a second course of 300,000 units of penicillin. He was discharged free from fever. The child was again admitted on 19-8-45 with fever, the symptoms were the same as before and a third course of penicillin was started on 21-8-45 and had 40,000 units to start with, then it was increased to 10,000 units per day up to 4-9-45, to a total of 770,000 units. On the whole the child had 1,595,000 units of penicillin. The temperature was controlled and the child was discharged on 5-9-45. He has been followed up and was free from fever 5 months after discharge.

*Summary*—A case of subacute bacterial endocarditis superimposed on congenital heart disease treated with penicillin. The first course (525,000 units) produced some improvement but relapsed; second course (300,000 units) also showed improvement but fever appeared again; a third course (770,000 units) controlled the fever and the patient was free from symptoms for 5 months after discharge.

*Case 2—Subacute bacterial endocarditis superimposed on patent ductus arteriosus.* S.B., Hindu,

female, aged 24 years, was admitted on 8-8-38 for irregular fever and palpitation. She was seen in January 1938 and was found to have patent ductus arteriosus without any symptoms. In April of the same year she noticed rise of temperature in the evenings accompanied with shivering and was treated with quinine in some other hospital. She was admitted in this hospital since the temperature was not controlled. *Physical examination* showed a thin individual, not anæmic, no clubbing, no cyanosis, no œdema. Circulatory system: pulse was 108 per minute with low volume and tension. The left border of the heart was in midclavicular line, and right border in right lateral sternal line. A systolic thrill was felt in the 2nd left intercostal space to the left of the middle line. A systolic murmur was heard in the mitral area, and a machinery murmur characteristic of patent ductus arteriosus was heard over the base of the heart more marked in the pulmonary area. Respiratory system showed nothing abnormal. Spleen was palpable just below the costal margin and liver was normal. While in the hospital she was running a temperature between 99 and 103°F, pulse rate between 86 and 108. Blood count: R.B.C. 8·29 million, W.B.C. 14,000. Smear did not reveal any parasite. Blood pressure varied from 92 to 116 systolic and 58 to 62 diastolic and was the same in both arms. Urine was normal.

The patient was put on sodium salicylate, but temperature was not controlled. Once her temperature shot up to 104°F. with a rigor. Repeated examination of the urine did not show anything abnormal, and culture was negative. From blood culture staphylococcus was isolated. She was discharged on 20-8-38 with a diagnosis of subacute bacterial endocarditis superimposed on patent ductus arteriosus. Later she was admitted in another hospital. The temperature could not be controlled, the patient gradually became weaker and died a few months later.

Summary—A case of subacute bacterial endocarditis superimposed on patent ductus arteriosus. She lived only for about thirteen months after the diagnosis was made.

*Case 3—Endocarditis superimposed on rheumatic mitral stenosis.* A.S.R., Hindu, male, aged 25 years was admitted on 4-6-36 with a history of pain in the joints, of one month's duration. He was married and has no children and gave a history of chronic dyspepsia of six months' duration. The fever started a month ago with pain in the left elbow joint and the other joints were involved one by one. *Physical examination* showed a moderately nourished individual, slightly anæmic, no jaundice, no œdema. Both the ankle joints were swollen and the right one was tender. Circulatory system: pulse 88 per minute, regular. Blood pressure 90/40. Apex beat was palpable in the 6th intercostal space just external to the midclavicular line. No thrills were felt. Systolic and presystolic murmurs were heard in the mitral area. Systolic murmurs were also heard in the aortic and pulmonary areas. Lungs showed occasional moist signs at the bases and liver and spleen were palpable below the costal margin. Blood smear showed leucocytosis. Stool showed no ova. Urine: specific gravity 1026, no albumin and no sugar.

Patient was put on 90 gr. of sodium salicylate a day from 9-6-36. He responded rapidly to the drug within 3 days but relapse occurred and the murmur became more marked. Urine examination at this time showed traces of albumin and centrifuged specimen showed nothing abnormal. Blood count done on 11-6-36 showed W.B.C. 7,000. Poly. 66, Lympho. 25, Mono. 4 and Eosino. 5 per cent. Widal reaction was negative for enteric group of organisms. Blood culture on 14-6-36 was negative. He was put on hexamine and bromides by mouth, the temperature was not controlled although the joint pains subsided. Urine on 16-6-36 showed nothing abnormal.

At 11 A.M. on 17-6-36, the patient became delirious; he started with a vacant look, the limbs became spastic for a minute and finally the whole body became flaccid in another 3 minutes. The pulse increased during the spasticity to 110 per minute, and five minutes later, complete hemiplegia of the left side with conjugate deviation of the head and eyes towards the right was observed. Plantar response was extensor on the left side and abdominal reflex was lost on the same side. At 10-30 A.M. *i.e.*, half an hour after the embolic phenomena, the patient's blood was taken for culture and streptococcus viridans was isolated. The patient died at 2-15 P.M. on 17-6-36. Postmortem was not available.

Summary—A case of suacute bacterial endocarditis superimposed on mitral steposis with embolic phenomena which resulted in hemiplegia on the left side and death.

*Case 4—Endocarditis superimposed on rheumatic mitral stenosis.* K.A., Hindu female, aged 16 years, was admitted on 15-5-45 with a history of fever of 4 months' duration. She used to have occasional attacks of pain in the knee joints but no sore throat. She used to complain of general weakness for which she consulted a doctor in December, 1944 when a systolic murmur was discovered in the mitral area. She was having a continuous temperature from that date varying between 99 and 103°F. *Physical examination* showed a poorly nourished individual with slight icteric tinge of the conjunctivæ, and inability to sit up due to weakness. She had a temperature of 100°F, pulse rate 110 and respiration 26 per minute. Heart was enlarged, left border just external to the midclavicular line, a systolic murmur was heard in the mitral and pulmonary areas and the 2nd sound was accentuated in the pulmonary area. Aortic and tricuspid areas were normal. Spleen was just palpable below the costal margin, lungs did not show anything abnormal, and no involvement of the joints could be discovered. Blood pressure 100/50. Urine: no albumin, no casts. Blood count: R.B.C. 2·5 million, W.B.C. 17,000. Differential count—Poly. 68, Lympho. 28, Eosino. 2 and Mono. 2 per cent.

Clinical diagnosis of subacute bacterial endocarditis was made. Radiological examination of the heart (Fig. 1) showed enlargement of the heart with slight enlargement of the left auricle in the right anterior oblique view with barium in the œsophagus.

Blood culture was negative. Examination of the eye on 31-5-45 did not show anything abnormal. For six days from 15-5-45 the patient was put on 100 gr. of sodium salicylate per day without any effect. Penicillin was started on 21-5-45 intramuscularly. She had 30,000, 70,000, and 20,000 units of penicillin on 21st, 22nd and 23rd respectively. The stock of penicillin ran short and so was not given on the 24th. The temperature that was gradually coming down rose up again on the 25th. Penicillin was again started on the 25th, 80,000 units per day. The temperature touched normal on the 1st of June. The dosage of penicillin was reduced to 20,000 units for 3 days. On the 3rd day the temperature shot up again. Penicillin was increased next day and afterwards there was no rise of temperature. The systolic murmur in the mitral area was better heard. Blood examination on 28-5-45: sedimentation rate 40 m.m. per hour, R.B.C. 3·8 million, W.B.C. 5,200. Differential count—Poly. 66, Lympho. 29, Eosino. 4 and Mono. 1 per cent. After 5-6-45 the patient had no fever. Injections of penicillin were continued up to 21-6-45, daily and stopped for one week. It was started again on 28-6-45, 40,000 units a day and continued up to 5-7-45. The patient was able to sit up and walk about in course of time and she put on weight. She had a total amount of 1,990,000 units of penicillin. Blood count on 19-6-45: R.B.C. 3·4 million. Differential count—Poly. 42, Lympho. 38, Mono. 13 and Eosino. 7 per cent. Blood Wassermann negative. Blood culture negative. She was discharged cured on 14-7-45, has been followed up and is free from fever for 8 months after discharge.

Summary—A case of subacute bacterial endocarditis superimposed on mitral stenosis. 100 gr. of sodium salicylate a day for 6 days had no effect on the temperature. With 1,990,000 units of penicillin the patient completely recovered and has been free from symptoms 8 months after discharge.

*Case 5—Endocarditis of the aortic valve with embolic phenomena.* P.P., Hindu, male, aged 21 years was admitted on 2-1-32 with a history of irregular fever ranging from 99° to 103°F. of two and half months' duration. Two years ago he had fever which lasted for about two months which according to him was treated as malaria. *Physical examination* showed enlarged heart and a systolic thrill and murmur in the aortic area. Blood smear showed only leucocytosis. Urine was normal. He was given quinine, salicylates and anti-streptococcal serum in another hospital. As there was no improvement he was transferred to King George Hospital on 2-1-32.

Physical examination on admission showed a moderately nourished individual with anæmia and clubbing of the fingers. Spleen was slightly enlarged, and liver just palpable below the costal margin. Heart: apex beat was visible in the 5th intercostal space just external to the midclavicular line, systolic thrill was felt in the mitral area, and systolic and diastolic murmurs were heard in all the areas except in the tricuspid. Pulse 84 per minute. Lungs showed diminished breath sounds over the right base with coarse crepitations. Urine: specific gravity 1012, albumin nil, sugar nil. Blood examination: smear showed microcytic anæmia but there were no parasites. R.B.C. 2·7 million. W.B.C. 10,240. Differential count—Poly. 79, Lympho. 16, Eosino. 2 and Mono. 3 per cent. Blood pressure 85/30. Sputum showed no tubercle bacilli even by the concentration method. Van den Bergh reaction negative. Widal on 8-1-32 negative. Blood culture negative. Radiogram of the kidneys on 12-1-32 nil abnormal. Urine culture on 12-1-32 negative. Radiogram of the chest on 14-1-32 showed few opacities at both the bases and slight enlargement of heart to the left. A nonlactose fermenting motile bacillus was isolated from the urine on 16-1-32. On 19-1-32, the patient developed œdema of the legs, his condition became weaker, and pericardial rub was heard in addition to the systolic and diastolic murmur over the base. Urine at this time showed plenty of R.B.C's., epithelial, fatty and granular casts showing evidence of embolism of the kidney. The patient developed dyspnœa and died at 2 P.M. on 23-1-32.

Postmortem conducted on the same day showed effusions in the pleura, peritoneum and pericardial cavities, endocarditis of the aortic valve (Fig. 2), hæmorrhagic pericarditis, partial collapse of both the lungs, multiple infarctions of both kidneys, multiple infarctions of spleen, passive congestion of liver and enlargement of the mesenteric glands.

Summary—A case of suacute bacterial endocarditis of the aortic valve running an irregular temperature for three months developed infarction of the kidneys while in hospital. Postmortem showed endocarditis of the aortic valve with multiple infarctions of the spleen and kidneys.

*Case 6—Endocarditis of the aortic valve with embolic phenomena.* M.A., Hindu, male, aged 50 years was admitted on 26-1-45 with history of breathlessness and inability to work, of one year's duration. He had persistent œdema for 4 months. Married and had 5 daughters, not addicted to alcohol, smokes 3 cigars a day. Three days before admission he had fever. There was no previous history of fever or pain in the joints. *Physical examination* showed a moderately nourished individual with ataxic gait and œdema of the hands and feet. Heart: left border was ½" external to the midclavicular line and right border just external to the right lateral sternal line. Systolic murmur was heard in mitral area and systolic murmur with accentuation of the 2nd sound in the pulmonary area. In the aortic area there was a systolic and a faint diastolic murmur. Blood pressure was 120/70, pulse regular, 78 per minute. Respiratory system was normal. Nervous system: intelligence was normal, cranial nerves normal, biceps, triceps, supinators, knee and ankle jerks were exaggerated, plantar response was extensor, abdominal reflexes were normal and there was no disturbance of sensation. Urine: specific gravity 1020, no albumin, no sugar and no casts. Blood Wassermann positive. Radiological examination of the heart (Fig. 4) showed slight enlargement both to the right and to left. There was no dilatation of the aorta but lung fields were hazy.

A provisional diagnosis of syphilitic meningomyelitis with syphilitic myocarditis was made. Beriberi was ruled out by the exaggeration of reflexes

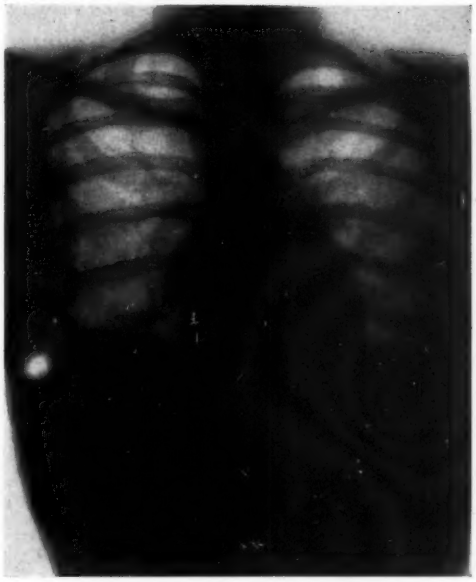

FIG. 1—RADIOGRAM OF THE HEART (CASE 4) SHOWING ENLARGED HEART AND PROMINENT PULMONARY CONUS.

FIG. 2—PHOTOGRAPH OF THE POSTMORTEM SPECIMEN OF THE HEART (CASE 5) SHOWING ENDOCARDITIS OF THE AORTIC VALVE. A CLOT IS SEEN IN THE AORTIC ORIFICE

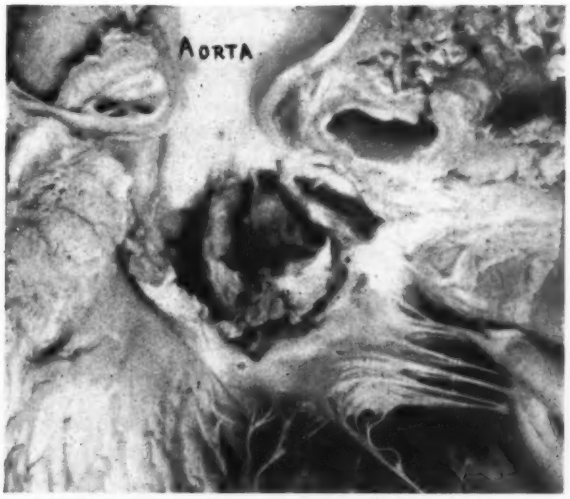


FIG. 3—MAGNIFIED VIEW OF SAME SPECIMEN AS IN FIG. 2 SHOWING ENDOCARDITIS OF THE AORTIC VALVE AND THE CLOT

FIG. 4—RADIOGRAM OF THE HEART (CASE 6) SHOWING ENLARGEMENT OF THE HEART, HYPERTROPHY OF THE LEFT VENTRICLE AND PROMINENT HILAR SHADOWS. THERE WAS NO DEFINITE EVIDENCE OF DILATATION OF THE AORTA

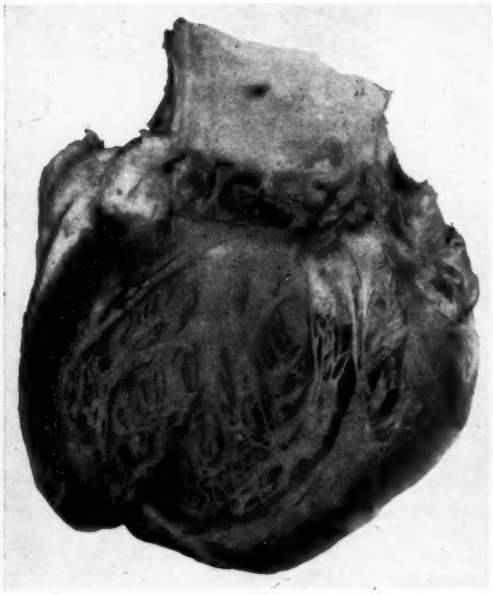

FIG. 5—PHOTOGRAPH OF THE POSTMORTEM SPECIMEN OF THE HEART (CASE 6) SHOWING ENDOCARDITIS OF THE AORTIC VALVE. A SLIGHT PATCH OF ENDOCARDITIS IS SEEN IN THE WALL OF THE AORTA ALSO. A SMALL VEGETATION IS OBSTRUCTING THE MOUTH OF THE LEFT CORONARY ARTERY

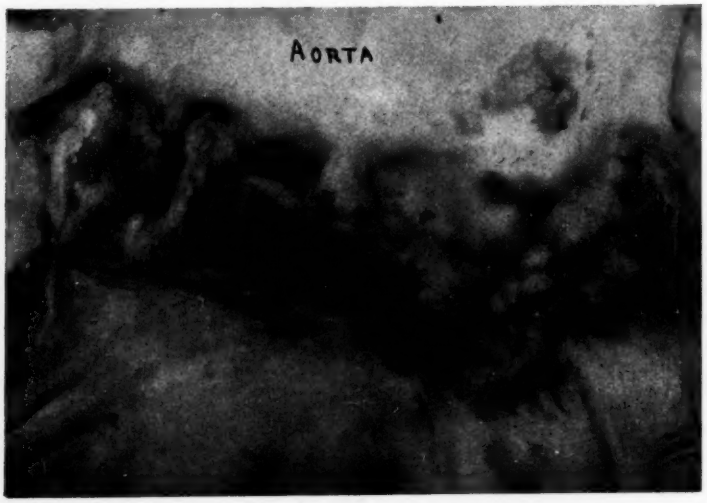


FIG. 6—MAGNIFIED VIEW OF SAME SPECIMEN AS IN FIG. 5 SHOWING ENDOCARDITIS OF THE AORTIC VALVE

and Babinski's sign. The patient was put on potassium iodide and he showed slight improvement. Blood pressure taken a few days later was 110/60. The patient complained of pain in the region of the precordium on 24-2-45 and in two minutes he fell down and died. The final clinical diagnosis was syphilitic myocarditis, syphilitic meningomyelitis and coronary thrombosis.

Postmortem showed generalised œdema, pericarditis and endocarditis of all the 3 cusps of the aortic valve (Fig. 5), congestion of the lungs, passive congestion of the liver and infarction of the spleen and kidneys. One of these vegetations was just over the region of the mouth of the left coronary artery, probably this might have caused coronary occlusion.

It is possible that the frequent embolic attacks of the spleen and kidneys might not have been severe and evidently has not attracted the attention of the patient. The complete absence of fever showed that the condition was chronic. The possibility of subacute bacterial endocarditis superimposed on an old syphilitic fibrosis of the aortic cusps cannot entirely be ruled out. The final diagnosis was subacute baterial endocarditis of the aortic valve with embolism and infarction of the spleen and kidneys. The patient had probably infarction of the spinal cord, not visible to the naked eye which clinically looked like syphilitic meningomyelitis.

Summary—A case of subacute bacterial endocarditis of the aortic valve in which the diagnosis was missed clinically and the patient died of coronary thrombosis. Postmortem showed endocarditis of the aortic valve and infarctions of the spleen and kidneys.

*Case 7—Subacute bacterial endocarditis with chronic interstitial nephritis.* K.R., Hindu, female, aged 40 years, was admitted on 22-6-44 with a history of irregular fever of two months' duration. Two years ago she was admitted into the hospital for chronic interstitial nephritis and was discharged relieved. The present fever was not controlled by salicylates or by sulpha group of drugs. She was married, had six children, all alive. *Physical examination* showed a fairly nourished individual with slight anæmia, no cyanosis, no œdema, no clubbing of the fingers. Heart was enlarged, the left border just external to midclavicular line, right border external to the right lateral sternal line. Auscultation revealed a systolic murmur in the mitral area and systolic and diastolic murmurs in the aortic and pulmonary areas. Spleen was just palpable below the costal margin. Respiratory system was normal. Blood pressure 150/88. Urine showed albumin, a few R.B.C's, and hyaline and granular casts. Blood showed leucocytosis. Examination of fundus showed narrowing of the arteries, exudative retinitis and retinal hæmorrhages. Blood urea was high (145 mg.) and urea clearance (standard) 8·2 per cent.

The patient was running a low temperature (99 to 101°F.) while in the hospital. A clinical diagnosis of subacute bacterial endocarditis superimposed on chronic interstitial nephritis was made. Blood culture showed streptococcus viridans. The patient was improving to a certain extent but the temperature was not controlled and the diastolic murmur in the aortic area became more pronounced. She was discharged relieved on 9-7-44. She was followed up and the temperature that was varying between 99 and 100°F. after discharge could not be controlled either by salicylates or by sulpha group of drugs. The patient gradually became worse and died about 5 months after discharge from the hospital.

Summary—A case of subacute bacterial endocarditis of the aortic valve superimposed on chronic interstitial nephritis. The temperature could not be controlled and the patient finally died of uræmia.

## Discussion

*Age and sex*—The youngest patient in the present series was 3 and the oldest 50 years. The youngest age reported was 1½ and the oldest 82 years. Walser (1928) reported the case of two babies shortly after birth showing streptococcus viridans septicæmia without any symptoms whatsoever, delivered by mothers suffering from subacute bacterial endocarditis.

There were 5 males and 2 females.

*Diagnosis*—The criteria for the diagnosis of subacute bacterial endocarditis as laid down by Horder (1926) are: (1) The presence of multiple emboli, (2) the signs of valvular disease, (3) the occurrence of fever and lastly (4) the discovery of the causative organism in the circulation by blood culture. Of these the first three are essential and the fourth one substantiates, but its absence does not negative the diagnosis of bacterial endocarditis. Libman and Friedberg (1941) consider these four as essential for diagnosis and includes one more *vis.*, a congenital heart lesion in addition to the signs of valvular disease. In all the cases in the present series except one, the diagnosis was made clinically. Irregular fever and the presence of cardiac murmurs were the two main features relied upon for diagnosis. Embolic phenomena were observed clinically in two cases, one producing hemiplegia of the left side and the other infarction of the kidneys. Positive blood cultures were obtained only in 3 cases. In 2 cases, streptococcus viridans was isolated and in the third, staphylococcus was isolated. In Case 6, patient aged 50, the diagnosis was not made during life and it belongs to the group of completely obscure cases described by Zeman (1945). The patient's history in this case never suggested any embolic phenomena and the diagnosis was not thought of during life. Postmortem revealed most interesting features. It is possible, that if a blood culture had been done, it would have been positive. The old infarctions are certainly indicative of embolic phenomena. Although it was not possible to demonstrate the embolic phenomena of the spinal cord, it is presumed that microscopic changes would have been noticed if carefully looked for. Zeman (*loc. cit.*) emphasises the difficulty of diagnosis of subacute bacterial endocarditis in old people, especially atypical forms, and says that in spite of long clinical experience and close observation there will still be left at least some cases of subacute bacterial endocarditis which will be disclosed only by postmortem.

*Bacteriology*—Bruce Perry (*loc. cit.*) has given an analysis of the organisms isolated from 1000 cases of bacterial endocarditis observed by different authors from 1899 to 1935. Of these 68 per cent were due to streptococcus and 24 of these were due to streptococcus viridans. Staphylococcus, pneumococcus and meningococcus were also observed but less frequently. In the present series, streptococcus viridans was isolated in 2 cases, in the 3rd staphylococcus was isolated. In some of the other cases blood cultures were negative. It has been said by different bacteriologists that the organism is not easy to culture from the circulating blood. Libman (1913) considers that there is a bacteria-free stage of the disease. In a few cases more than one organism has been isolated, streptococcus, staphylococcus and streptococcus viridans with hæmolytic streptococcus (Cotton, Horder, Phipps and Howell). It has been suggested that there are inhibiting substances in the blood which prevent the growth of the organisms in cultures. Wright does not agree with this view. He thinks that negative blood culture shows only that at the time the blood was taken there were no organisms in circulation. Frequent blood cultures with larger quantities of blood could have resulted in greater number of positive results in our series.

*Experimental animals*—Lloyd Jones (1936) has produced bacterial endocarditis in experimental animals by injection of streptococcus pyogenes or streptococcus fæcalis. The vegetations produced by streptococcus fæcalis were more massive than those produced by streptococcus pyogenes. Infarctions were also seen in experimental animals. In one of the animals autopsy showed no endocarditis but old infarctions of the kidneys were present and he suggested that this might be one of those cases of healed bacterial endocarditis in experimental animals.

*Pathology*—Bruce Perry (1936) quoted all the available data regarding the involvement of different valves published by several authors (Clawson, Horder, Lenhartz, Libman, Morrison, Phipps and Thayar).

| | |
|---|---|
| Mitral valve | 428 |
| Aortic | 337 |
| Tricuspid | 68 |
| Pulmonary | 24 |
| Congenital heart disease | 11 |
| TOTAL | 868 |

In the present series of 7 cases, mitral valve was involved in 2, aortic valve in 3, and congenital heart disease was present in 2 cases.

The chief predisposing factors are rheumatic endocarditis (80 per cent) and congenital heart disease (5 per cent) consisting of bicuspid aortic valve, interventricular or interauricular septal defects, patent ductus arteriosus and coarctation of aorta (White, 1944). Occasionally more than one valve may be involved. Postmortem examination was available only in two cases in this series and in both the aortic valve was involved. In one (Case 5) hæmorrhagic pericarditis was present in addition and multiple infarctions of the kidneys and spleen were present. A recent infarction of a kidney occurred 4 days before death and was diagnosed clinically. In the other (Case 6) there was pericarditis in addition to endocarditis of the aortic valve and the vegetations were big enough (Fig. 5) to produce obstruction of the coronary artery at its mouth which resulted in the sudden death of the patient. Infarctions of the kidneys and spleen were present in addition. The question whether the changes in the spinal cord are a result of embolic phenomena or are a result of syphilitic meningomyelitis is doubtful. Subacute bacterial endocarditis can be superimposed on syphilitic aortic regurgitation but the clinical evidence in this patient was more against than in favour of syphilitic aortic regurgitation.

Smith (1937) reported the co-existence of syphilitic aortitis and bacterial endocarditis in one patient. Boyd (1940) thinks that bacterial endocarditis superimposed on syphilitic endocarditis occurs more often and found 14 cases in a series of 105 cases of bacterial endocarditis. Koletsky (1943) reported 5 cases of bacterial endocarditis with cardiovascular syphilis. Zeman criticizes these findings, as evidence of rheumatic infection was present in 4 of these cases and he thinks that syphilis is not a predisposing factor in bacterial endocarditis. Touroff (1943) in a series of 51 cases of patent ductus arteriosus, found 2 cases with bacterial endocarditis and says that subacute bacterial endocarditis constitutes a perpetual danger to a patient suffering with bacterial endocarditis.

In one case of the present series (Case 2) the patient had repeated attacks of fever and the temperature remained normal only for a few days, relapsing again. She finally succumbed nearly 1½ years after the diagnosis was made.

The endocardial lesions have a tendency to extend from the valve to the mural endocardium and are frequently seen in the wall of the left auricle.

*Treatment*—The three stages in the treatment of subacute bacterial endocarditis are: the 1st stage up to 1935 when practically there was no treatment whatsoever and whatever treatment was given was only symptomatic. The 2nd stage of sulphanilamide therapy (Klee and Romer, 1935 *loc. cit.*) when some successful results were reported but the mortality was still high. The 3rd stage *i.e.*, the stage of penicillin therapy which started in 1942 (Flippin *et al*).

Spontaneous cures of subacute bacterial endocarditis have been reported. Libman and Friedberg (1939) reported 22 spontaneous cures in a series of 1500 cases. Lichtman (1943) reported 3 spontaneous recoveries in 1096 cases. Except for these spontaneous cures, the mortality was very high. When once the diagnosis of bacterial endocarditis was made the prognosis was considered grave and invariably the patient died, either immediately or a few months later.

Klee and Romer (*loc. cit.*) reported disappointing results in 5 cases treated with prontosil I. In 3 of these cases streptococcus viridans was isolated, in the 4th nonhæmolytic streptococcus, and in the 5th the culture was negative. All the patients died. Waxman (1938) reported a case which showed temporary improvement with sulphanilamide and temporary reduction in the bacteria by culture but the patient

finally died. Recoveries have been reported by Lichtman (1939), Galbreath and Hull (1942), and Bunn (1944). Paullin and McLoughlin (1945) summarised the results of these observations and brought the figures up to 24 cures in a series of 535 patients. Later sulphanilamide was used with heparin and 7 recoveries have been reported in a series of 109 cases. Solomon (1941) reported 5 cures in 22 cases with hyperpyrexial treatment in combination with sulphanilamide. Two cures have been reported by Lichtman (1939). We tried sulphanilamide only in one case with disappointing results.

*Penicillin*—Flippin *et al* (1942) treated unsuccessfully a patient with 225,000 units of penicillin in seven days.

Keefer *et al* (1943) reported disappointing results with treatment of 17 cases of subacute bacterial endocarditis with penicillin. Only 3 cases showed temporary improvement but 2 of them relapsed.

Dawson and Hobby (1944) treated 10 cases of bacterial endocarditis due to nonhæmolytic streptococcus. Two cases recovered, one case showed temporary improvement, two cases died and in the remaining five cases there was no effect.

Herrell *et al* (1944) used penicillin in 4 cases of subacute bacterial endocarditis, none of the cases responded although the blood culture became negative in one case.

Loewe *et al* (1944) reported successful results in 7 cases of bacterial endocarditis, 6 of these were superimposed on rheumatic heart disease and the 7th superimposed on congenital heart disease. Six of these were due to streptococcus viridans and the 7th due to pneumococcus but in all these cases penicillin was given in higher doses. Heparin was also given in addition. They suggested that in some of these cases preliminary administration of sulphanilamide hastened the recovery.

Swenney (1945) reported failures in 5 cases, the total dosage being 1,400,000 to 2,600,000 units.

Paullin and McLaughlin (1945) treated with penicillin 6 cases of subacute bacterial endocarditis. Positive blood cultures were obtained in all these 6 cases, 3 of the cases were failures and the remaining 3 were cured. Some of these patients received sulpha drugs in addition, but the cultures remained positive during and after the course of this treatment. Large doses of 3 to 4 million units of penicillin were employed in these cases.

Flippin *et al* (1945) reported 20 cases of bacterial endocarditis treated with penicillin, 16 of these showed subsidence of the infection, 12 were alive at the time of reporting, and 4 of these were free from infection and died sometime later of heart failure. Three did not respond to therapy. Still higher doses were used in these cases: 300,000 units a day for 14 days. In cases of highly resistant organisms, they used penicillin X with success.

Chatterjee and De from Calcutta (1945) reported failure in 3 cases treated by them. In one case 600,000 units showed immediate improvement but after the stoppage of penicillin, relapse occurred and the patient died.

Bloomfield and Halpeon (1945) followed up 18 consecutive cases. 11 of them were free from symptoms for 3 to 11 months and the remaining 7 from 12 to 17 months after treatment. In addition they observed that the treatment must be continued for two months or longer irrespective of the daily dosage. To give small doses in the beginning and to increase the dosage afterwards does not seem to be a sound procedure since the organisms might develop increased resistance to penicillin. Further, congestive heart failure, coronary occlusion and cardiac irregularities such as extra systoles, auricular flutter and auricular fibrillation were observed during the course of treatment with penicillin. From a series of 35 cases, Dawson and Hunter (1946) reported 30 cures with penicillin. They were followed up for an average period of fourteen months, some of them required larger doses and one case was given 92,000,000 units in repeated courses. Hudson *et al* (1946) observed that larger number of cures could be obtained when 60,000 units are given every three hours for 28 days.

During the first three days the patient (Case 4) had penicillin and showed a decrease in temperature. Since the stock of penicillin ran short, it was not given one day, then temperature began to rise again. Subsequent administration of penicillin controlled the fever and the patient had 1,990,000 units of penicillin intramuscularly. Unfortunately, blood culture was not positive in this case before treatment. She has been followed up for 8 months after discharge and she is free from all symptoms.

In the 2nd case (Case 1) a child with congenital heart disease, 525,000 units of penicillin controlled the fever but relapse occurred and a 2nd course of 300,000 units also controlled the fever, but the fever relapsed again and a 3rd course of 770,000 units brought down the fever. On the whole the child had 1,595,000 units. The child has been followed up for 5 months after discharge, and is free from all symptoms. In the last course the dosage was practically double, *i.e.*, 100,000 units per day, evidently in the earlier courses the dosage was insufficient.

## Summary

(1) The literature on bacterial endocarditis is reviewed.

(2) Seven cases of subacute bacterial endocarditis are described: 2 showed endocarditis of the mitral valve, 3 of the aortic valve, and in the remaining two it was superimposed on congenital heart disease.

(3) Recovery occurred in 2 cases both treated with penicillin. One patient had two courses and the other three.

(4) Postmortem was available in 2 cases and both showed endocarditis of the aortic valve with infarctions of the spleen and kidneys.

## Acknowledgments

Our thanks are due to Dr. T. Bhaskara Menon for the postmortem, to Dr. N. G. Pandalai for the bacteriological investigations and to Dr. G. I. Benjamin for the radiograms.

(*Concluded at foot of col. 1, page 82*)

## THE NUTRITION PROBLEM IN THE PUNJAB*

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### INTRODUCTION

During the months of January and February, 1946 the problem of food supply in India has been an urgent one and it is the main preoccupation of central and provincial administrations. Cereals form the great bulk of Indian diets, providing 80-90 per cent of total calories. Owing to failure of rains throughout India there is a threat of general and local shortage of cereals, notably rice, involving danger of starvation in the greater part of the country. There are no alternative foods available in sufficient quantities to replace cereals. A new position has thus been created with regard to the problem of nutrition in India. It has come into the foreground of public attention and the Governments are preparing, as never before, to take action in this field. In fact India is in a very critical condition. There is reason to believe that to meet the exigencies of the situation the Government of India is launching a uniform policy.

In a country of the size of India which includes the most varied population groups with different dietary habits it is impossible for any one individual or group to study problems of nutrition in all parts of the country simultaneously. The relevant information should be available for each district. In the absence of sufficient data and in view of the emergent conditions, information should at least be available for individual provinces. It is with this aim that I propose to discuss the nutrition problem in the Punjab.

The problem has been dealt with in this paper under the following heads: 1. Available land and food supply. 2. Diet surveys. 3. Nutritional surveys. 4. Suggestions for improvement of diet.

### AVAILABLE LAND

The total area of the province is 63·4 million acres, of which 31·7 million acres were under cultivation in the year 1944. The population of the Punjab in that year was estimated at 29,749,896. Thus cultivated land works out at 1·073 acres per head. The question arises whether there is sufficient land or not. In this connection results of certain studies by workers in the United States of America are of particular significance. In these investigations (Stiebeling and Ward, 1923) four diets were drawn up as follows:—

(*a*) An "emergency restricted diet." This diet consisted largely of cereals and was designed to tide very poor and destitute people, *e.g.*, the unemployed, over a comparatively short period of privation.

(*b*) An "adequate diet on minimum cost." This was a more expensive diet, including less cereals and rather more milk, meat, fruit and green vegetables.

(*c*) An "adequate diet at moderate cost." This was roughly similar to (*b*) but was richer in milk and other nutritious fruits.

(*d*) A "liberal diet." In this diet the proportion of cereals was reduced to 100 lbs. per year, a quart of milk per day was included, and meat, fruit and green vegetables were added to maximum quantities.

Diets (*b*), (*c*) and (*d*) are similar in energy value while the caloric value of diet (*a*) is slightly less.

The amount of land per capita required (in the U.S.A.) to produce these diets was calculated by an agricultural expert (Baker, 1934). The acreage was as follows:—

| *Diet* | *Acres per capita.* |
|---|---|
| (*a*) .. .. .. | 1·2 |
| (*b*) .. .. .. | 1·8 |
| (*c*) .. .. .. | 2·3 |
| (*d*) .. .. .. | 3·1 |

As compared to the above, cultivated land per head in the Punjab is 1·07 acres. These figures show that we have not sufficient land to produce even an "emergency restricted diet." Agricultural conditions are very different in the Punjab. Because of better and scientific methods of cultivation used in United States of America per acre field is comparatively greater in America than in India. Water logging, growing decrease in soil fertility and increasing population are additional unfavourable factors operating in the Punjab.

### FOOD SUPPLY

The Punjab is normally a large exporter of cereals. These exports consist in the main of wheat, but also include rice, millet and barley. It is for this reason that the Punjab has been called the granary of India. But let us study the position more carefully. In Chart I are given annual production of cereals—

*Read at a meeting of the I.M.A., Lahore Branch, on 2nd March, 1946.

(*Concluded from page 81*)

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*Note*:—The names of the other authors mentioned in the paper are from the quotations by the authors of original articles.

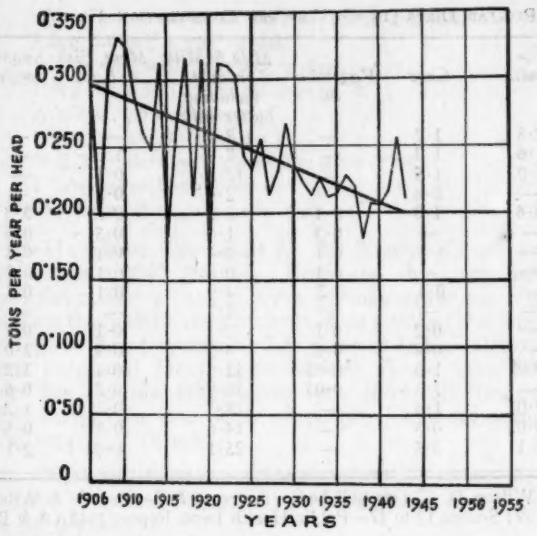


CHART SHOWING ANNUAL PRODUCTION OF THE SEVEN FOOD GRAINS VIZ., WHEAT, RICE, JOWAR, BAJRA, BARLEY, MAIZE AND GRAM, PER HEAD OF POPULATION FROM 1906 ONWARDS.

wheat, rice, jowar, bajra, barley, maize and gram per head of population from 1906 onwards. It is quite apparent from the chart that the amount of available cereals per head is decreasing every year. This is due to the rapidly increasing population of the province. From 1920 to 1945 the population figures have risen from 20·2 million to 29·5 million *i.e.*, an addition of over 3½ lacs each year. The present position regarding cereals is that if we reckon the cattle and human requirements, the Punjab is a deficit province. Now let us examine the situation in another way. In Table I are given the estimated requirements of different foodstuffs to ensure a balanced diet for all inhabitants of the Punjab according to the yard sticks provided by the United Nations Organisation at the Hot Springs Conference in 1943 and the Indian Nutrition Advisory Committee.

These figures are compared with the statistics of production collected from the Punjab Agricultural Department.

The above estimates also show that the Punjab is self-sufficient in cereals and pulses only, even when the requirements for cattle are not taken into consideration. It further shows that we in this province are very badly in need of what are known as the protective foods.

TABLE I—SHOWING ESTIMATED ANNUAL REQUIREMENTS (IN MILLION TONS) FOR HUMAN CONSUMPTION

| *Foodstuff* | *United Nations' Organisation (F & A) Standard (Plan 1)* | *Nutrition Advisory Committee (India)* | *Statistics of production collected from Pb. Agricultural Dept.* |
|---|---|---|---|
| Cereals .. .. | 3·5 | 4·2 | 6·34 |
| Pulses .. .. | 0·36 | 0·9 | 1·16 |
| Milk .. .. | 7·11 | 3·0 | 4·67 |
| Green leafy vegetables .. | 1·18 | 1·2 | No estimate |
| Nonleafy vegetables .. | 4·46 | 1·8 | do. |
| Meat and fish .. .. | 1·35 | 0·6 | Meat—No estimate Fish—0·001 |
| Butter and ghee .. | 0·75 | 0·3 | 0·17 |
| Vegetable oils .. | — | 0·3 | No estimate |
| Sugar .. .. | 0·42 | 0·6 | 0·58 |
| Fruits .. .. | 1·18 | 0·9 | 0·18 |
| Eggs .. .. | 6,526 (million by count) | 700 (million by count) | 49·7 (million by count) |

## FAMILY DIET SURVEYS

In all, 17 diet surveys have so far been carried out in this province. Diet surveys have revealed the nature of diet consumed in the various parts of the Punjab and their adequacy or otherwise in quantitative and qualitative sense. Regarding the method of carrying out such surveys and the information they supply I shall quote from the Nutrition Advisory Committee Report.

"In a typical survey a quantitative investigation is made for all the food consumed by a simple group of 15-30 families in a given area from 10-30 days. Intake of various foodstuffs per adult male or consumption unit is worked out and the composition of the diet in terms of food factors *i.e.*, proteins, mineral salts, vitamins etc., is calculated. It is to be observed that while there is inevitably a considerable margin of error in diet surveys because of the circumstances in which they are made and for numerous other reasons, they provide the most satisfactory means of obtaining a true picture of dietary habits and information about dietary defects."

TABLE II—SHOWING PRINCIPAL FOODSTUFFS IN OZ. PER ADULT MALE UNIT PER DAY IN BALANCED DIET

| | *Recommendation of U.N. Conference on Food & Agriculture* | | *Recommendation in Health Bulletin No. 23* |
|---|---|---|---|
| | Plan I | Plan II | |
| Cereals .. .. | 10·03 | 8·49 | 15·0 |
| Pulses (mature leguminous seeds & nuts) | 1·06 | 0·58 | 3·0 |
| Leafy vegetables .. | 3·47 | 6·75 | 4·0 |
| Nonleafy vegetables (starch-rich tubers, roots and other vegetables & fruits) .. | 13·12 | 15·05 | 6·0 |
| Fruits (vitamin C-rich fruits .. .. | 3·47 | 4·15 | 2·0 |
| Fat .. .. | 2·22 | 2·22 | 2·0 |
| Vegetable oils .. | .. | .. | .. |
| Milk & milk products | 20·93 | 23·15 | 8·0 |
| Meat, fish (flesh products .. .. | 3·96 | 5·21 | .. |
| Eggs (number) .. | 0·6 | 0·75 | .. |
| Sugar & jaggery .. | 1·54 | 1·54 | .. |

TABLE III—SHOWING PRINCIPAL FOODSTUFFS IN THE PUNJAB DIETS (IN OUNCES PER CONSUMPTION UNIT)

| Diet Surveys | Cereals | Pulses | Leafy vegetables | Non-leafy vegetables | Fruits | Ghee | Vegetable oil | Milk & Milk products including butter milk | Meat, Fish & Eggs | Sugar & Jaggery |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 17·4 | 1·9 | — | 4·6 | 2·5 | 1·2 | — | 8·7 | — | — |
| 2 | 19·8 | 1·0 | — | 5·1 | 1·6 | 1·3 | — | 7·8 | 1·5 | — |
| 3 | 17·8 | 1·6 | — | 4·2 | 1·0 | 1·5 | — | 12·3 | 0·1 | — |
| 4 | 22·4 | 2·7 | — | 3·3 | — | 0·4 | — | 2·4 | 0·7 | — |
| 5 | 18·0 | 1·6 | 3·4 | 3·3 | 0·4 | 1·0 | 0·1 | 8·3 | 0·6 | 3·3 |
| 6 | 26·7 | 1·7 | 0·6 | 1·9 | — | — | 0·3 | 1·6 | 0·5 | 0·6 |
| 7 | 27·2 | 2·7 | 0·2 | 0·8 | — | — | 0·1 | 3·4 | 0·1 | 0·1 |
| 8 | 23 | 0·9 | 0·4 | 0·7 | — | — | 0·1 | 0·8 | 0·1 | 0·1 |
| 9 | 27·1 | 1·8 | 0·9 | 1·2 | — | 0·1 | 0·2 | 4·0 | 0·1 | 0·1 |
| 10 | 27·3 | 1·8 | — | 1·5 | — | — | — | 1·7 | — | — |
| 11 | 32·3 | 2·1 | — | 1·9 | — | 0·2 | 0·1 | 2·2 | 0·1 | 0·1 |
| 12 | 26·1 | 1·5 | 1·7 | 6·9 | — | 0·4 | 0·1 | 4·5 | 0·9 | 1·0 |
| 13 | 32·1 | 1·1 | 0·07 | 3·5 | 0·07 | 1·0 | 0·03 | 11·6 | 0·1 | 1·2 |
| 14 | 32·6 | 2·6 | — | 2·3 | — | 1·3 | 0·03 | 10·9 | 0·2 | 0·6 |
| 15 | 33·7 | 1·9 | 0·8 | 3·1 | 0·01 | 1·3 | — | 18·5 | 0·1 | 1·2 |
| 16 | 34 | 0·4 | 0·1 | 1·7 | 0·03 | 0·5 | — | 14·6 | 0·1 | 0·6 |
| 17 | 27·7 | 3·4 | 2·1 | 7·9 | 3·1 | 3·5 | — | 25·1 | 0·02 | 2·1 |

*N.B.*:—Source 1 to 4—Ahmad & Gore (1938); Source 5—Wilson D. C. (unpublished); Source 6 & 7—Shourie & Wilson (unpublished); Source 8 to 11—Public Health Dept. Report 19 39; Source 12 to 17—Public Health Dept. Report 1943 (A & B).

TABLE IV—SHOWING CALORIC VALUE AND CHEMICAL COMPOSITION OF THE DIETS IN THE PUNJAB

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Calories .. .. | 2903 | 2468 | 3029 | 2923 | 3576 | 3231 | 3854 | 4104 | 4321 | 3822 | 5055 |
| Protein (gm.) .. | 82·1 | 55 | 76 | 84 | 102 | 109 | 130 | 140 | 150 | 135 | 148 |
| Fat (gm.) .. .. | 23·3 | 14 | 17 | 21 | 28 | 37 | 49 | 59 | 68 | 35 | 141 |
| Carbohydrate (gm) .. | 614·7 | 531 | 638 | 606 | 721 | 613 | 732 | 751 | 799 | 737 | 795 |
| Calcium (gm.) .. | 0·35 | 0·2 | 0·42 | 0·4 | 0·55 | 0·85 | 1·30 | 1·26 | 1·76 | 1·44 | 2·34 |
| Phosphorus (gm.) .. | 1·69 | 1·5 | 1 | 2·6 | 3·3 | 2·77 | 3·61 | 3·64 | 4·03 | 3·66 | 4·07 |
| Iron (mgm.) .. | — | 40 | 48 | 72 | 86 | 48 | 55 | 56 | 63 | 53 | 66 |
| Vitamin A & Carotene (I.U.) .. .. | — | 602 | 1100 | 822 | 984 | 3316 | 1879 | 2100 | 3071 | 1679 | 5636 |
| Vitamin $B_1$ (I.U.) .. | — | 919 | 1224 | 1270 | 1727 | 1282 | 1642 | 1692 | 1759 | 1701 | 1523 |
| Vitamin C (mgm.) .. | — | 3 | 7 | 2 | 6 | 96 | 11 | 10 | 19 | 8 | 50 |

Table II recorded the allowances of principal food stuffs in the diet recommended by the United Nations' Conference on food and agriculture as also allowances recommended by the Director, Nutrition Research Laboratories, Coonoor (South India), in Health Bulletin No. 23 for an average adult male. In Table III are given the intake of important groups of food stuffs as determined in various surveys. Most of the families investigated belong to the poorer classes and their diet is typical of that consumed throughout the year by millions in the areas in which the surveys were carried out.

Perusal of the table shows that in addition to his staple cereal a person in the Punjab consumes only small quantities of pulses and vegetables, consumption of meat, fish and eggs taken together does not often exceed 1·5 ounces daily, leafy vegetables are eaten in small quantities while the consumption of milk and milk products is inadequate. Fruit is a rare ingredient in the diet.

In Table IV are shown the chemical compositions of various diets consumed by different groups.

Mean caloric intake per consumption unit per day ranges from 3000 to 5000 calories. It may be of interest to note that caloric intake for the Punjab is comparatively higher than for the rest of India. Due to his experience in South India, Aykroyd recommends 2600 calories per consumption unit per day for an adult Indian. He further suggests that in the case of hard working agriculture ryots as well as for North Indians "a somewhat higher scale would be appropriate." There is no definite recommendations regarding caloric intake per consumption unit per day for an average Punjabee. We find that the diet surveys show a figure from 3000 to 4000 calories per consumption unit. It is interesting to note that this finding falls in line with the caloric consumption in ancient Punjab. The following interesting anecdote may give some idea regarding the caloric intake in "the good old days". It is recorded that Bhagat Kabir once felt hungry and rebelled against God. When in this state he is reported to have recited the following in Punjabi. Below is an English translation:

"A hungry man cannot perform service;
Take back this rosary of thine.
I only ask for the dust of the Saint's feet.
Since I owe not any man.
O God, how shall I fare if I am shamed before thee.
If Thou give me not of Thine own accord, I will beg for it.
I beg for two *seers of flour.

*One old Seer—2/5 Seer.

A quarter of a seer of clarified butter and salt.
I beg for half a seer of dal.
Which will feed me twice a day.
I beg for a bed with four legs to it.
A pillow and a mattress;
I beg for a quilt over me.
And Thy slave will cheerfully serve Thee.
I have never been covetious.
Thy name alone becometh me."

The above diet asked for by Bhagat Kabir provides about 3990 calories. From the above anecdote and the results of diet surveys we may draw one conclusion that caloric requirements of an average Punjabee is higher than persons in other parts of India. Central and provincial rationing authorities should take this fact into consideration when they think of bringing the Punjab in line with other provinces regarding the supply of cereals.

Total protein consumption appears to be satisfactory but the proportion of animal proteins leaves something to be desired.

The question arises: what is the optimum amount of protein? In answer to this question the opinion of American workers (U.S. Department of Agriculture, Miscellaneous Publication No. 546) may be quoted:

"How much food protein it would be best for each of us to eat in the interest of nutritional well-being is a question which does not admit of a simple conclusive answer. Several circumstances combine to delay the prompt reaching of real consensus of expert opinion on this point. Relatively long term researches into the more permanent effects of different levels of protein feeding may still be needed in order clearly to distinguish science from tradition in the interpretation of clinical experience. Also, the fact that the different food proteins contain different proportions of the individual nutritionally essential amino-acids inevitably means that what has hitherto been called the protein problem must be a whole group of amino-acids problem. In this latter field of research current work is making distinct scientific advances.

"Researches of many workers—Rose, Lewis, Jones and others have greatly extended our knowledge of the fate and functions of individual amino-acids in our bodies and their quantitative distribution in our foods. With the aid of this knowledge investigators are turning renewed attention to such questions as the extent to which we can depend upon foods furnished directly by the land and how the supplementing of these cheaper forms of proteins by more costly proteins of animal origin can be managed with maximum economy and efficiency."

I wish we, in this country, where larger proportions of vegetable proteins are consumed and greater variety of pulses is available, should take up this line of research.

*Mineral Salts*—Calcium intake of most of the groups except those examined in Kangra Valley appears to be adequate. The adequacy is on the assumption that the total content of calcium in the foodstuffs is available and is assimilated. During recent years much work has been carried out on the phytic acid content of wheat and it is claimed by some that whole wheat diet contains an anti-calcifying factor. Here again there is an unsolved problem for future research. Some light can be thrown on this by supplementing the diet of a group of growing children with calcium salts for some time and comparing the average growth, height and weight, with the results obtained from similar control groups.

Phosphorus content in the diets appears to be satisfactory.

Iron—The amount of iron in the diets consumed also appear to be satisfactory but we must take into consideration the fact that iron of different foods is not equally available to the body. In analysing the data, total iron in a foodstuff rather than available iron has been taken into consideration. There is no clear conception of the available iron.

*Vitamins*—Vitamin A—The United Nations' Conference on Food and Agriculture recommended the intake of 5000 international units of vitamin A per consumption unit per day. Judged on this standard vitamin A requirement has not been fully met except in one group.

Vitamin B—Vitamin $B_1$ and $B_2$ group contents of the diet could be taken as adequate as the diets are based on whole wheat and pulses which are quite good sources of $B_1$ and most members of $B_2$ group.

Vitamin C—The intake of vitamin C on the whole is not adequate.

Family diet surveys also reveal that our diets are lacking in many essential food factors.

## Deficiency Diseases

The incidence of deficiency diseases is another criterion which can with advantage be applied to a population for evaluating its nutritional status.

In Table V are quoted statistical figures of cases of deficiency diseases treated in the hospitals and dispensaries of the Punjab. It may be pointed out that not all such cases seek treatment, as the hospital facilities are not adequate. Nor can it be said that all such cases are correctly diagnosed as suffering from specific deficiency states. Even so, the available information throws an interesting light on the nutritional state of the people.

Table V—Showing Incidence of Deficiency Diseases

| | *Name of deficiency disease* | *No. of patients treated annually (average of 1934-42)* |
|---|---|---|
| 1. | Goitre .. .. .. | 32,939 |
| 2. | Other diseases due to deficiency or disorders of nutrition .. .. | 21,907 |
| 3. | Rickets .. .. .. | 2,897 |
| 4. | Scurvy .. .. .. | 1,976 |
| 5. | Osteomalacia .. .. .. | 1,019 |
| 6. | Xerophthalmia .. .. .. | 582 |

As already stated too much reliance should not be placed on the figures given above. It was therefore planned to carry out a survey to record the incidence of deficiency diseases in Lahore. Accordingly the following six schools were selected in consultation with the school medical officer:

1. Primary School, Kucha Ghian near Kashmiri Bazar, Lahore.
2. Primary School, Kucha Saduan, Lahore.
3. Primary School, Kucha Babian inside Shahalmi Gate, Lahore.
4. Primary School, Wachhowali, Lahore.
5. Primary School, Kucha Mohammadi near Railway Godown, Lahore.
6. Primary School, Faiz Bag, Lahore.

Of the above six schools 4 schools are situated in thickly populated areas in the city while the last two are in an area less thickly populated. In all 1589 children were examined.

Malnutrition, undernutrition or subnutrition are vague terms which have different shades of meanings for different workers so these were not taken as the criterion. In the present survey clear cut and definite signs of deficiency diseases were taken as the criteria. The following deficiency diseases were recorded:—

*Phrynoderma*—Dryness of the skin has often been noted amongst famine population. It is due to vitamin A deficiency.

In the present investigation outer surfaces of the arms were examined for phrynoderma, only the presence of marked degrees of condition were noted *i.e.*, cases which gave to the finger tip the sensation of passing over a rough surface or pin heads. Mere dryness of the skin which was found to be present in a very high percentage of children examined was not recorded.

*Xerophthalmia*—This condition is also attributed to lack of vitamin A in the diet. In the present investigation we have included cases showing "Bitot's spots" only and various degrees of dryness of the conjunctiva have not been taken into account. "Bitot's spot" the whitish or yellowish foamy patches on the conjunctiva are easy to observe and is a convenient sign in routine examination by non-ophthalmologists.

*Smokiness of Conjunctiva* has often been noted in a famine but has so far not been definitely associated with any specific dietary essential.

*Angular Stomatitis*—This is associated with riboflavin deficiency. In the present investigation only marked degrees of angular stomatitis were recorded.

Incidence of *spongy gums* and *rickets* was also recorded.

TABLE VI—SHOWING INCIDENCE OF DIET DEFICIENCY DISEASES IN LAHORE CHILDREN

| | *Phrynoderma* | | *Bitot's Spots.* | | *Angular Stomatitis* | |
|---|---|---|---|---|---|---|
| | No. | Percentage | No. | Percentage | No. | Percentage |
| 1. | 229 | 0·9 | 3 | 1·3 | 22 | 9·5 |
| 2. | 323 | 3·4 | 2 | 0·6 | 21 | 6·5 |
| 3. | 189 | — | 2 | 1·1 | 3 | 1·6 |
| 4. | 233 | 1·3 | 4 | 1·7 | 3 | 1·7 |
| 5. | 249 | 2·0 | 8 | 3·2 | 24 | 9·6 |
| 6. | 366 | 1·4 | 8 | 2·1 | 41 | 11·2 |
| Total | 1589 | 1·7 | 27 | 1·7 | 114 | 2·2 |

Table VI shows the incidence of phrynoderma, angular stomatitis and Bitot's spots in children examined in the various schools. 10·5 per cent of children examined showed signs of deficiency diseases. This percentage will rise considerably if the number of children showing smokiness of the eyes is also included.

Regarding the gum condition nearly 80-90 per cent of children had gingivitis but they could not be labelled as clinical scurvy cases because of the earlier findings (Day and Shourie, 1943) which showed that gingivitis in this part of the country could not be controlled by the administration of ascorbic acid.

*Anæmia*—Cases of anæmia were quite common. As no data regarding the hæmoglobin content of the blood could be collected definite views regarding this condition cannot be put forward. On the question of anæmia recent work carried out in the Punjab especially the investigation undertaken by Wig shows that nutritional anæmia is quite frequently encountered.

On the basis of evidence put forward in this paper it can be stated that the Punjab diet is by no means as satisfactory as is commonly supposed.

## SUGGESTIONS FOR THE IMPROVEMENT

It is well-known that poor income or lack of purchasing power is the root cause of inadequate nutrition of a large number of workers and their families. It is mostly an economic problem. But there can be some improvement if the available resources are properly tapped.

Suggestions for improving the diet of an individual with limited means:—

1. There must be an increased use of green leafy vegetables. Green leafy vegetables are cheap, easily available and highly nutritious. The inclusion of these vegetables in adequate quantities in diets will bring about improvements with very little, if any, additional cost. Leafy vegetables are rich sources for the supply of organic acids, and mineral salts while their bulk stimulates peristalsis. They are also rich in carotene and vitamin C. Since *ghee* (animal fat containing vitamin A) is scarce and costly, leafy vegetables are of special importance as a source of carotene (provitamin A). It is now an accepted dictum that a well-balanced dietary contains a liberal amount of fresh leafy vegetables.

2. We should try to include as much milk and milk preparations as our income permits.

3. Preparation and cooking of foodstuffs must be done with a proper scientific knowledge. Cooking affects the nutritive value of food; for instance, there is loss of mineral salts in boiling. Potatoes when boiled lose about 18 per cent of their mineral matter and 6 to 8 per cent of their protein. Ascorbic acid, riboflavin and nicotinic acid dissolve readily in water and therefore pass out into the water in which foods are cooked. If cooking is defective a properly planned diet may still be inadequate. It is the cook who makes a diet fit for ingestion—palatable and appetising—but the art of cooking is more than the mere production of a tasty dish attractively served. A good cook must know how to conserve food values. In passing it may be worth while to note the following suggestions for saving vitamins (U. S. Department of Agriculture, Year Book, 1939, p. 295):

*(Concluded at foot of col. 2, page 95)*

# TREATMENT OF RELAPSING CASES OF MALARIA

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Treatment of relapsing and chronic cases of malaria is still a baffling problem for the physicians inspite of the introduction of efficient chemotherapeutic remedies. Prolonged use of the compound 'amyl-acridine' (2-chloro-7-methoxy-5-(ω-diethyl amino-iso-amyl-amino-acridine) named atebrin, and renamed as mepacrine in B.P. has been recently reported to suppress further attacks of malaria (Findlay, Markson and Hoiden, 1944). Quinine, however, has been found tc be useless in this respect (Franchi and Santel, 1935). The experience of the medical practitioners in this country would testify to the fact that mepacrine used at the ordinary dosage during acute attacks, frequently gives rise to untoward symptoms, particularly of the psychotic type (Chakravarti and Misra, 1946). Naturally, prolonged administration of this drug is not likely to find favour with them.

Some controversy has raged recently regarding the efficacy of organometallic compounds in the treatment of malaria. Nunno (1935) reported treatment of malarial cases with antimonium tartrate injected intravenously. The purpose of the treatment was to stimulate the reticulo-endothelial system, which brought about a 'true mobilisation of the parasites" with febrile attacks during the early doses. But after the 4th or 5th dose fever went down and the spleen got rapidly reduced. The therapy so carried, cannot however be considered satisfactory as relapses occurred even after a course of several injections.

The use of organo-arsenical drugs in malaria has been more extensive than antimony preparations, though available reports are somewhat conflicting. Murphy (1929) reported good results with intravenous injections of sodium cacodylate. Goldman (1938) found that over 90 per cent of the cases treated with a single injection of Mapharsen intravenously were permanently cured of malaria. Cleveland and Turvey (1939) though agreeing with him suggested a larger number of injections for cure. On the other hand, Young and McLendon (1939) failed to observe with Mapharsen eradication of the infection in any one of the cases of induced quartan malaria (*P. malariæ*); even the viability of the parasites were not affected. Further studies in Simian malaria by Das Gupta and Siddons (1944) showed that neither Novarsenobillon (N.A.B.) nor Mapharside gave satisfactory results in treatment (*cf.* Kay, 1945). Recently, however, Stewart (1945) has suggested that a combination of quinine with Mapharside makes a more efficacious therapy than quinine alone.

During the study of the anti-malarial activity of the compound, 2-chloro-7-methoxy-5-( ω-diethylamino-butyl)-amino-acridine called 'butyl acridine' (Siddons and Bose, 1944) against *P. knowlesi* infection in monkeys it was casually observed that relapses of malarial fever, which usually occurred after treatment, were prevented in those animals who had any subsequent injections of Mapharside.* Finding this observation to be interesting from the point of view of practical therapeutics, it was considered worthwhile to follow the study in relapsing cases of human malaria. All previous observations had been carried with arsenical preparations for intravenous use. These being considered more toxic and inconvenient for general administration, the present studies have been carried with an intramuscular preparation of organically combined arsenic. The results of the investigation carried on the efficacy of Arseno-Sulph, a brand of sulpharsphenamine, B.P., in the treatment of human malaria is being incorporated in the body of this paper.

* Unpublished data.

## METHODS AND MATERIALS

During these studies, special care was taken to select only cases of malaria having repeated relapses inspite of treatment with various schizonticidal drugs. Most of the patients had history of relapses for over a period of 6 months to 3 years. The treated cases have been divided into several groups according to the nature of treatment given. A control group under treatment with quinine or 'amylacridine' was kept for observation of a few further relapses, before final treatment with Arseno-Sulph. In the former groups, the method of treatment was as follows:—After confirming the diagnosis with thick and thin films, the case was primarily put on any one of the schizonticides, such as quinine, 'amyl-acridine' or 'butyl acridine' for 5 days. During this period the fever subsided, and the peripheral blood got free from parasites. After a rest for another 3 days, treatment was instituted with Arseno-Sulph (I.R.I), a brand of sulpharsphenamine, B.P. A preliminary test dose of 0·06 gm. was given in debilitated cases in order to test the sensitiveness of the patients to arsenic.

Afterwards, bi-weekly injections were started with the following doses; 0·12, 0·18, 0·24, 0·36 gm. generally, and sometimes 0·48 gm. as well. From the day of injection and on two following days, alkalies were administered in such doses as to keep the urine on the alkaline side. The dosage of the schizonticides employed are given in the protocol of Table I. As it has been previously observed (Bose, Ghosh and Rakshit, 1944) that 'butyl acridine' can act at a lower dosage of 30 mgm. thrice daily for 5 days, the same dosage was also employed in this investigation.

A total of 20 cases (all of *P. vivax* infection except two) have been treated by this combined method of therapy with schizonticide followed by arsenical drug. All the persons were male Bengalees except two up-country men. The number of cases treated in each group and the results of such treatment are given in their respective protocols in Tables I and II.

## DISCUSSION AND CONCLUSION

The results of the combined treatment of relapsing malarial cases with schizonticides and Arseno-Sulph (sulpharsphenamine B.P.) seems to be in conformity with the findings of Goldman (*loc. cit.*), and Cleveland and Turvey (*loc. cit*). It can be seen from the tables that no relapse has yet been observed in any one of the cases who have undergone the full course of the

TABLE I—SHOWING THE RESULT OF COMBINED TREATMENT OF RELAPSING CASES OF MALARIA WITH ORAL SCHIZONTICIDE AND ARSENO-SULPH (I.R.I.) INTRAMUSCULARLY.

| Case No. | Age | Approx. no. of relapses & period of suffering | Total dose of schizonticide in gm. | Doses of Arseno-Sulph in gm. | Result of combined treatment | Relapse after treatment | Subsequent treatment | Period of observation | Final result |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Group I (Amyl-acridine and Arseno-Sulph) | | | | | |
| 1. | 25 | 6; for about 1 yr. | 1·5 | 0·06, 0·12 0·18, 0·24 0·36, 0·48 | good | nil | nil | 1 yr. | cured |
| 2. | 20 | 8; for about 1 yr. | 1·3 | 0·06, 0·12 0·18, 0·24 0·36 | " | " | " | 1 1/3 yrs. | " |
| 3. | 23 | 4; for about 5 months | 1·5 | " | " | " | " | 2 yrs. | " |
| 4. | 24 | 5; for 9 months | 1·3 | 0·12, 0·18 0·24, 0·36 0·48 | " | " | " | 6 mo. | " |
| 5. | 30 | 5; for 6 months | 1·3 | 0·12, 0·18 0·24, 0·36 | " | " | " | 3 " | Apparently cured |
| | | | | Group II ('Butyl-acridine' and Arseno-Sulph) | | | | | |
| 6. | 16 | 12; for 1½ yrs. | 0·45 | 0·06, 0·12 0·18, 0·24 | " | " | " | 1½ yrs. | Cured |
| 7. | 21 | 3; for 4 months | 0·75 | 0·12, 0·18 0·24, 0·36 0·48 | " | " | " | 2 yrs. | " |
| 8. | 10 | 10; for 1½ yrs. | 0·45 | 0·06 0·12 | " | " | " | 2 1/3 yrs. | " |
| 9. | 25 | 10; for 1½ yrs. | 0·9 | 0·12 | not followed | Yes, one | Quinine injection | — | not known |
| 10. | 24 | 8; for 1 year | 1·4 | 0·06 0·12, 0·18 | good | nil | nil | 2 yrs. 2 mo. | cured |
| 11. | 18 | 30; for 3 yrs. | 0·9 | 0·06 0·12 | " | " | " | 2 yrs. | " |
| | | | | Group III (Mixed group treated with 'amyl acridine' (A) or 'butyl acridine' (B) or quinine (C) during relapses and Arseno-Sulph after last relapses | | | | | |
| 12. | 28 | 4; for 3 yrs. | C-5·0 A-1·5 B-0·9 | 0·06, 0·12 0·18, 0·24 0·36, 0·48 | good | nil | nil | 2 yrs. | cured |
| 13. | 36 | 3; for 6 months | C-1·5 A-1·0 | 0·06 | not satisfactory | yes one | C-1·5 A.S.- 0·06, 0·12 0·18, 0·24 0·36 | 2 mo. | no more relapse. Being followed |
| 14. | 45 | 8; for 10 months | C-4·0 A-1·5 | 0·12, 0·18 0·24, 0·36 | good | nil | nil | 7 mo. | cured |
| 15. | 35 | 7; for 1 year. | C-5·0 B-1·5 | 0·12, 0·18 0·24, 0·36 0·48 | " | " | " | 9 mo. | " |
| 16. | 27 | 3; for 6 months | C-5·5 | 0·06, 0·12 0·18, 0·24 0·36 | " | " | " | 8 mo. | " |

therapy. The only case (Case No. 13) which gave a single relapse, was partially treated and after a full course of arsenic has not yet shown any tendency to relapse. No toxic manifestation or untoward symptom was detected in any case. This was possibly due to particular care being taken in assisting the renal functions by the administration of alkalies. Considering the chronicity of the illness and the large number of attacks of fever before commencement of treatment the results with Arseno-Sulph therapy appears to be remarkable. It must be noted that the timing of the injections was also carefully chosen, being a period when the parasites have been so powerfully overcome by the schizonticides as to disappear from the peripheral blood. It is quite probable that the endothelial parasites, which are now considered to be the cause of repeated relapses in malaria (Kikuth, 1943; Short and Menon, 1940) were so dosed by the anti-malarial drugs that they were unable to defend against a fresh onslaught of arsenic. Though the number of cases reported is small yet the results justify the use of Arseno-Sulph or probably any other intramuscular

TABLE II—SHOWING CONTROL GROUP—HAVING RELAPSES INSPITE OF TREATMENT WITH QUININE (C), OR 'BUTYL-ACRIDINE (B), AND SUBSEQUENTLY TREATED WITH ARSENO-SULPH (A.S.) AND AMYL-ACRIDINE (A)

| *Case No.* | *Age* | *Approx. no. of relapses & period of suffering* | *Total dose of schizonticide in gm. during each relapse* | *Doses of Arseno-Sulph.* | *Subsequent relapses* | *Drug in subsequent treatment in gm.* | *Period of observation after Arseno-Sulph therapy* | *Result of treatment* |
|---|---|---|---|---|---|---|---|---|
| 17 | 30 | 3; for 2 months | C-0·45 | nil | 4 in 6 months | A-1·5<br>A.S.-<br>0·06, 0·18<br>0·24, 0·36 | 10 months | Cured |
| 18 | 23 | 2; for 2 months | C-5·0 | „ | 3 in 2½ months | A-1·5<br>A.S.-<br>0·06, 0·12<br>0·18, 0·24 | 2 months | Cured |
| 19 | 32 | 2 in 1 month | C-(inj.)—<br>C-2·0 | „ | 2 in 2 months | A-1·5<br>A.S.-<br>0·06, 0·12<br>0·18, 0·24 | 2 months | Being followed |
| 20 | 19 | 15 in 2 years. | C-5·0 | „ | 2 in 1½ months | C-5·0<br>A.S.-<br>0·06, 0·12<br>0·18 | 3 weeks | Under treatment |

arsenical preparation in conjunction with anti-malarial remedies in tackling the relapsing cases of malaria. It would also be interesting for chemists to search for new acridine or quinoline compounds with arsenic attached to their nuclei, so as to combine in one the synergistic effect of arsenic with anti-malarials. (*cf.* Banerjee and Ghosh, 1946).

## SUMMARY

1. A total number of 20 cases of chronic relapsing malaria have been treated with schizonticides followed by intramuscular injections of Arseno-Sulph (I.R.I.)

2. No relapse has been observed in any one of the cases, which underwent a full course of arsenical therapy.

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## PLASMA TRANSFUSION*

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Plasma transfusion is one of the most important scientific advances in the realm of medicine in the present century. It is the natural result of search for a fluid which could nullify the evil effects of severe blood loss. Blood of course is such a fluid par excellence and no wonder that even ancients used blood as a tonic. As transfusion technique was unknown in those days, so blood was used in massaging the body. Pharaohs of Egypt used to take bath in the blood collected from their enemies and slaves. Blood was also drunk and as a matter of fact, modern hæmoglobin syrups are nothing but modified blood.

Shortly after the discovery of circulation of blood by Harvey in 1661, Richard Lower performed the first operation of blood transfusion by connecting the artery of one animal to the vein of another. Then Denys, a French physician, practised the art of blood transfusion from one person to another and while in some cases the results were marvellous, in others the patients began to pass dark urine and died. Denys was tried and blood transfusion was banned by law in England and France. In other parts of Europe blood transfusion continued with variable results, for which no satisfactory explanation seemed to be forthcoming.

In 1901 Landstiner of Vienna made an epochal discovery of two different agglutinogens in R.B.C. which were called A and B and corresponding agglutinins in human serum and divided the human beings into four main groups according to the agglutinogen present in their blood. He was awarded Nobel prize for this discovery. Since then blood transfusion has become much safer and the disasters encountered by earlier workers have been explained.

The discovery of subgroups of A, types M and N and factors P and Rh, the last in 1940 by Landstiner and his associates have added materially to our knowledge and made blood transfusion still more safe.

As the result of these discoveries, blood transfusion became very popular but still there was difficulty of bringing the donor to the bed-side. In Russia this problem was solved by using cadaver blood taken ¼ to 6 hours within death from otherwise healthy persons dying accidently. In other countries citrated blood stored in refrigerators began to be used as it was found that blood stored in this way remained usable for 7 to 28 days. In World War No. I and for many years afterwards citrated blood remained the main article for transfusion.

Use of plasma for transfusion was recommended as far back as 1918. In the same year it was used in cases of influenza with good results. But World War No. II is mainly responsible for bringing plasma transfusion in general use. Plasma has got obvious advantages over blood.

1. No typing is necessary.
2. There is no danger of transmitting syphilis or malaria.
3. Plasma can be kept at room temperature for a pretty long time—about a year.
4. Plasma can be obtained as a waste product.
5. Transport and administration are easy.

Dried plasma like liquid plasma was prepared in 1940 and at once became more popular as:

(*i*) It was less bulky (about 8 per cent of liquid plasma).

(*ii*) It was more durable, almost indefinitely.

(*iii*) It was easier to transport.

(*iv*) More concentrated plasma could be given as in some cases administration of proteins increases osmotic tension and fluid passes from the tissues to the circulation.

In the Punjab liquid plasma and serum were prepared for the first time by the late Col. Hayes. Since May 1945, liquid plasma is being prepared in the Pathology Laboratory of the K. E. Medical College, Lahore, under the guidance of Dr. A. N. Goyle. Here citrated blood is kept in the cold storage and used in Mayo and other hospitals when necessary. After a week the unused blood is processed into plasma. That is, it is pooled, clarified and filtered.

Bottles showing hæmolysis (Hb. more than 5 mgm. per 100 c.c.) or containing excessive lipoids are discarded. Supernatant plasma from the remaining bottles is pooled into one or more Winchester quart bottles of 2 litre capacity by the help of a suction pump, fixed to the water tap through a closed system of bottles and tubes, so that plasma does not come in contact with air or fingers. Air which replaces plasma is passed over an 18 feet long copper coil heated over a gas stove and passed through a sterilised cotton filter. After pooling, the plasma is allowed to stand in the cold storage for 48 hours or longer. During this time most of the agglutinins become absorbed by the respective agglutinogens.

Clarification and filtration are done together. The pooled plasma is passed through a clarifying chamber into a serum chamber. Clarifying chamber is an air-proof copper vessel with its inner surface tin-plated, containing a pad prepared from rag pulp and blotting paper. The serum chamber is also made of copper and tinned inside. It is fitted with a gauge which registers the internal pressure in pounds. When all the plasma has entered the serum chamber it is forced through two Seitz filters into 500 c.c. transfusion bottles. Pressure is applied by the help of a foot pump, air being passed through heated copper coil and a clarifying chamber. When a bottle is full, its screw is tightened and sealed with a mixture of beeswax and resin heated to 160°C. As an additional precaution against contamination a piece of cellophane is tied over the cap. Small samples are taken from the pooled plasma and from each bottle of filtered plasma and cultured on agar, broth and cooked meat media. The culture tubes are examined after 7 days. Generally all samples of pooled plasma show growth. If the media tubes containing filtered plasma show no growth, the bottles which were lying in the cold storage

*Read at the Scientific Session of the XXII All-India Medical Conference, Amritsar, December 1945.

for these seven days are taken out and kept at ordinary room temperature for 10 days as a further precautionary measure. If the bottles do not show any sign of contamination they are issued for use. If a large number of culture tubes show growth, the plasma is refiltered and the same process repeated.

During processing strictest asepsis, more thorough than that for a surgical operation, must be maintained The defensive mechanism of a surgical patient may be able to overpower a few micro-organisms which may accidentally enter a wound. But plasma is an excellent culture medium and even a single *bacillus subtilis* may play havoc with a plasma bottle. So all the apparatus must be thoroughly sterilized. The room must be kept scrupulously clean. The table is covered with a rubber sheet whose upper surface is washed with an antiseptic lotion and after drying, it is covered with sterilised towels. The workers use sterilised overalls, masks and rubber gloves and no outsider is allowed to enter the room during processing. Immediately after pooling and filtration, the whole apparatus is completely dismantled and every piece is thoroughly washed in tap water. Rubber tubes are cleaned inside with a tape to remove any clot and along with glass tubes and rubber bungs are boiled for one-half hour in plain water and after two or three experiments in 2 per cent soda carb. lotion. Transfusion bottles deserve special treatment. They are filled with sulphuric acid bichromate mixture (pot. bichromate 100, sulphuric acid 250 and water upto 1000) and kept for 24 hours. Then they are washed thoroughly with plain water and finally with distilled water and baked in the hot air case for one hour at 160°C. Then the whole apparatus is loosely packed in trunks and autoclaved at 20 pounds pressure for one hour. Just before packing all the parts are rinsed in distilled water and their open ends covered with cotton wool and tied.

Plasma should be stored at 80°F or between 70°F and 90°F. But we store it at room temperature. Fibrin floccules appear in plasma but it does not matter. It is strange that fibrin never appears in citrated blood or in pooled plasma. Its passage through asbestos filter seems to cause the appearance of fibrin. Various methods have been advocated to prevent fibrin formation, but they are not practicable and may endanger the safety of plasma. A simple and harmless method to get rid of fibrin is still our chief problem.

*Contamination—B. subtilis* is the chief contaminating micro-organism. Sometimes *staphylococcus* or *diphtheroids* singly or together are the culprits. On referring to the old records I find that the late Col. Hays used plasma contaminated with *B. subtilis* and *staphylococcus* without any harm to the patient and I have seen plasma contaminated with *B. subtilis* being used at least in one patient who was none the worse for it. Still the rule is never to use contaminated plasma. When sterility is in doubt the plasma bottle should be returned to the issuing centre. Sometimes the presence of fibrin causes confusion. But in non-contaminated plasma there is at least a portion which is quite transparent.

## Uses

It is chiefly used in surgical emergencies, in shock and hæmorrhage, instead of, or, in addition to, whole blood. Normal saline, glucose saline, pectin, isinglass and gum saline have also been used as blood substitutes, but plasma is superior to all of them. In burns and crushed injuries, where only fluid portion of blood has been lost, plasma is superior to blood. If a large quantity is to be transfused and blood available is more than 8 days old, it is better to use plasma and later on blood, if oxygen-carrying elements are found to be essential, than only old whole blood, because in the latter case though there is good immediate recovery yet some time later the kidney is unable to deal with pigment derived from hæmolysis inevitable after whole blood and oliguria or anuria may follow.

Even where fresh blood is available sometime is likely to be lost in grouping and cross matching and it is best to give the first bottle of plasma to avoid delay.

A pulse rate of 100 per minute or more and a blood pressure (systolic) 80 mm. of Hg. or less are indications for transfusion, but in shock pulse rate and blood pressure are not good guides. General condition of the patient, cold ashen skin, volume of the pulse, thirst and restlessness are more important. If it is decided to wait, pulse rate, blood pressure and general condition should be recorded every 15 minutes. Falling blood pressure and pulse volume with increasing pulse rate and worsening of the general condition are indications for transfusion. In severe injuries, crushed injuries, abdominal injuries, compound fracture especially of femur, transfusion is indicated. In chest injuries whole blood should be given and plasma avoided. Head injuries generally do better without transfusion or plasma concentrated 5 times may be given in 40 c.c. dosage. In burns if 1/6th or more of skin is involved, plasma transfusion is indicated. Two to four or more pints may be required in 24 to 48 hours.

If laboratory facilities are available, a check should be kept of red cell count, hæmoglobin percentage and serum protein content. Generally we have to depend upon general condition of the patient, relief of tissue œdema and blood pressure.

Plasma is also useful in surgical operations, where considerable blood loss is unavoidable. Also in severe hæmorrhage without shock.

Slow continuous drip at about 40 drops a minute is the best rate to avoid sudden overloading of circulation. In urgent cases the rate should be quicker, first pint in ten minutes or less and the next pint in 20 minutes and so on. Later on, if necessary, plasma transfusion should be continued at a drip rate.

A gauze or metal filter must be incorporated in the administering set to keep back fibrin and soaps.

*Bad after-effects*—In most cases nil. In some cases there is rigor, shivering and slight rise of temperature. Use of pyrogen-free distilled water in preparing citrate solution and in rinsing the apparatus

before autoclaving go far to reduce the incidence of these reactions. A small percentage of reactions still remains which is probably due to antigenic differences in plasma. There is danger of transmission of virus diseases and a few cases of jaundice due to infective hepatitis, occurring a few weeks after plasma transfusion have been recorded.

Plasma has also been used in cases of hypoproteinæmia due to chronic parenchymatous nephritis and other forms of albuminuria, or due to starvation, septic states or after surgical operations especially on the intestines. Hypochloræmia after operations on stomach and fibrinogenopenia are other conditions where plasma has been successfully used.

Recently Professor Cohn of Harvard University has fractionated plasma into different proteins and used them for different purposes.

(1) Albumin about 60 per cent of plasma protein and mainly responsible for osmotic activity of plasma and therefore invaluable as the main constituent of a volume-restoring fluid.

(2) Immune bodies of the globulin class, especially globulin which have proved valuable in prophylaxis of measles and infective hepatitis. In this the antibody concentration is 15 to 20 times that of natural pooled plasma. In an epidemic of measles, when used in 2 or 2·5 c.c. dose, he was able to protect 80 per cent of young susceptible and exposed children.

(3) Fibrinogen on which clotting property of blood depends has been used as fibrin foam in neurosurgery and in plastics.

Plasma has also been used in skin grafting.

Before finishing, a few words must be said about serum. Serum is prepared from non-citrated blood. It is more difficult to pool but easier to filter than plasma. Quantity obtained from the same amount of blood is less than plasma. Plasma was preferred to serum which was reported to give rise to serious reactions in some cases. But now the general opinion is that one is as good as the other.

Plasma does not contain any red cells or white cells so it is quite useless or may be harmful in cases of anæmia or agranulocytosis where whole blood must be used.

It will not be out of place to mention that in processing plasma, red cells are discarded and no use has been found for them. It has been suggested that after separating plasma the red cells should be suspended in normal saline and re-injected into the donor. In this way a donor could donate blood more frequently, but there are obvious difficulties in adopting this course. In the end it must be stated that though plasma is a good substitute for blood, the complete blood substitute has yet to be found.

ACKNOWLEDGMENT

I should like to acknowledge the help and able guidance kindly given to me by Professor A. N. Goyle in plasma processing work.

## OINTMENTS

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Ointments are one of the oldest forms of medication. The Ebers Papyrus of ancient Egypt gave directions for the incorporation of various drugs in goose grease for external application. Ancient Hindus also used various types of ointment called *pralep* as mentioned in Charak and Sushrut Sanhita. Galen developed cold cream for ointment bases. Various other vehicles—fats, oils and greases have been used throughout the ages for the incorporation of the antiseptic drugs for the cure of sores, wounds and cuts etc. But even up till now very little is known as to their behaviour with respect to the body surfaces with which they come into contact so that their use is to a large extent empiric.

The animal fats were unsatisfactory from a pharmaceutical standpoint because they readily developed rancidity. Addition of preservatives retarded but did not prevent rancidity. Perhaps because of this, petrolatum replaced them in most ointments.

The most widely used base to-day is petrolatum. It is stable and is compatible with most medicaments. But it has no tendency to absorb water—not even as much as the natural fats. So its use is sometimes contra-indicated. Certain types of dermatitis of the hand should not, as is often the case, be covered with greasy ointment because this prevents evaporation of perspiration and may cause secondary infection.

As early as 1881 Koch observed that phenol, when dissolved in oil or alcohol showed less bactericidal action than it did in aqueous solution. In 1895 Breslauer, reported upon the bactericidal effects of ointments and concluded that cold cream and lanolin were the best ointment bases for antiseptics. A few years later Eldred showed the presence of bacteria or moulds in thirty of the fifty samples of official ointments and bases which he tested. In 1929 Reddish and Wales tested twelve ointments of U.S. Pharmacopœia and fourteen of the National Formulary and found that only five of the former and six of the latter ointments exhibited antiseptic properties. They concluded that because of the influence exerted by the base it was impossible to predict the antiseptic action of the ointment from the antiseptic value of its constituents.

Gershenfeld and Miller, Prout, Eddleman and Harris, Burnside and Keuver, Craw and Lee, Folley and Lee, all have shown that phenol when incorporated in various greasy bases in 2 per cent concentration is not bactericidal in action. Bryan found that at least 10 per cent of phenol was necessary to produce bactericidal potency when incorporated in greasy bases. This was subsequently confirmed by Clerk in 1939 when in a series of tests he showed that a 10 per cent phenol ointment in petrolatum failed to produce a measurable zone of inhibition on a 10 per cent serum agar plate. In recent years ideas of external medication with ointments have been challenged by evidence indicating that a greasy ointment is ill-advised in the

treatment of many skin conditions because the serious discharge of a wound is aqueous in character and it can neither find exit through a greasy barrier nor can medication in the greasy base reach the diseased tissue. Furthermore it is contended that a layer of a greasy ointment prevents the escape of heat from an inflamed area.

Where there is perspiration or a serous discharge, a hydrophilic ointment base is essential so that perspiration acts as a medium and not as a barrier. Such a base should consist entirely or in large part of water soluble material.

### The Ideal Base

Mumford states, "An ideal base would be one which acted with equal efficiency on dry and oily skins, which could be removed with water instead of olive oil or liquid paraffin and which could suspend within itself water soluble and fat soluble chemicals and transfer them to the skins. In certain cases a non-hydrophilic occlusive base might be desired. Usually, however, a hydrophilic base is desirable. These considerations led to the evolution of emulsion type of ointments where water may be the continuous phase (oil-in-water type) or where water may remain in the dispersed phase (water-in-oil type).

The advantages of emulsified ointments compound to those not emulsified are many.

Firstly, it has been shown that they do not interfere with the normal function of the skin secretions as do those which are non-emulsified. Secondly, they are most effective when applied. Thirdly, they are more acceptable cosmetically. Fourthly, they are more effective as bacteriostatic and bactericidal agents when tested by acceptable procedures.

The question is what will be the type of emulsion most suitable for use.

Much interest has been shown in recent years by the pharmaceutical and medical professions in the so-called absorption bases. Fischler in a study of emulsion types of ointments found that water in oil emulsions had greater penetrating properties than pure fats and petrolatums.

In investigating the antiseptic potency of various bases with ammoniated mercury and phenyl mercuric nitrate, they found that the ointments made with water-holding bases had a distinctly higher potency than those without water.

Duemling studied wetting agents and their effect on skin penetration. He found that fats alone penetrated chiefly about the hair follicles to a depth just below the skin. Fats in combination with wetting agents, however, penetrated to the base of the hair follicles rapidly, soon penetrated to a depth of 4 mm. below the skin surface and then spread out through the fibro-fatty tissue.

Below is given a typical example of a creamy (W/O) type of base which has served as a very good base for acridine antiseptics:

| | |
|---|---|
| Lanolin .. .. | 5 |
| Paraffin wax .. .. | 5 |
| Beeswax .. .. | 12·5 |
| Liquid paraffin .. | 52·5 |
| Distilled water .. .. | 25 |

The oily mixture is heated to 70°c in a water-bath and the water heated to the same temperature is gradually added to the oil mixture. After the whole quantity of water has been added, the stirring is continued for half an hour more and finally the mixture is triturated in a mortar.

A typical absorption type of ointment base as prepared by Johnston and Lee is supplied by the following;

| | |
|---|---|
| Cholesterol .. .. | 3 |
| Cholesterol stearate .. | 3 |
| Anhydrous lanolin .. | 25 |
| White petrolatum .. .. | 69 |

Heat the petrolatum and lanolin to about 50°C, add cholesterol and cholesterol stearate and stir until dissolved. Stir occasionally until cooling.

The base easily takes up 300% of water. It will emulsify much more water than this. Its spreading quality is quite satisfactory. Johnston and Lee investigated these bases as vehicles in W/O type emulsions for ointment use. They concluded that aside from extemporaneous use, they are sensitive to temperature changes and are not stable. Other attractive looking cream bases also did not suit well. The most logical approach to formulating stable ointment emulsions is with the oil-in-water type.

Inherently this emulsion system possesses a stability that has much to recommend it. It is possible to incorporate large amounts of water without upsetting the equilibrium of the two phases. The higher percentage of water allows greater diffusion of the antiseptic from the ointment base and enhances its efficiency when applied. From a medical point of view Wise and Wolf in discussing the parasiticidal action of sulphur on the skin conclude that this action is in all probability due to the formation of $H_2S$. It seems natural that this would be favourably influenced by a high water content in an ointment emulsion. All these considerations led to the development of so-called 'water-washable' ointment bases which act as a medium through which heat can be conducted away from the wound, serous discharge can pass and medication can reach the diseased area.

As a matter of fact the suitability of an ointment base should be judged by whether it (1) would produce oil in water emulsions, (2) would produce emulsions that are stable to most medicaments the pharmacist might be called upon to incorporate in it, (3) would be economical to use, (4) would permit the use of at least a 50 per cent water concentration, (5) would lend itself to both extemporaneous stock preparations, (6) would be readily available.

As an outcome of these considerations various oil-in-water type ointment bases have been prepared in recent times. A typical one of these is the following prepared by Gibson *et al*:—

| | |
|---|---|
| Sodium lauryl sulphate .. | 0·5 |
| Cetyl alcohol .. .. | 8·0 |
| Cacao butter .. .. | 6·5 |
| White petrolatum .. | 20·0 |
| Water .. .. | 65 |

The base is first prepared without water. The cetyl alcohol, petrolatum and cacao butter are melted over a water bath, sodium lauryl sulfate then added and the whole stirred until cool. In using this base 50 per cent of the finished ointment is to be water. If for example 10 per cent of ammoniated mercury is to be prepared, 50 gms. water, 10 gms. ammoniated mercury and 40 gms. of the base is used. In our quest for a washable ointment base having all the qualities required as above, we have been able to prepare one with the following composition:

| | | |
|---|---|---|
| (*i*) | Cetyl alcohol .. | .. 8 |
| | Beeswax .. | .. 1 |
| | White vaseline | .. 25 |
| (*ii*) | Turkey red oil | .. 2 |
| | Glycerine .. | .. 10 |
| | 6% Kaolin suspension | .. 54 |

The melted cetyl alcohol mixture (*i*) is added to (ii) heated in a water-bath at 60°C and stirred mechanically. It is then stirred for 10 minutes more, allowed to cool and triturated in a mortar.

Recently sulfanilamide type compounds are being incorporated into ointment bases for topical application. These substances are bacteriostatic and not bactericidal. So precaution should be taken so that these ointments are sterile lest these contain any pathogenic organism which cannot grow in presence of sulfanilamide but which are not killed. As such living organisms by coming in contact with the wound may give rise to toxic symptoms. The p-hydroxybenzoic esters are being used as preservatives in these ointments to counteract the action both of pathogenic organisms as well as moulds and fungi.

### Reaction of Ointment

The pH of the ointments must be determined by the nature of the antiseptics to be incorporated and the stability of the base which has been selected under various hydrogen-ion concentrations. The pH of the skin is near about 6·2. So it is better to keep the pH of any ointment within the range of 6 to 7·5. All the medicaments that are used in ointments will not be compatible in a single base. So different bases may have to be used with different medicaments. But the same base will be compatible with a good number of medicaments. A universal ointment base is the aim of the pharmacists but it has not yet been achieved.

### Standardisation

It will not be out of place to mention here something about the process by which the bacteriostatic activity of the ointments are measured. Sterile meat extract agar is melted and poured into sterile petri dishes, 15 c.c. of agar being added to each dish. Into each dish is pipetted 0·1 c.c. of a suspension of the organism from a twenty-four hour broth culture. After the inoculated agar hardens, the ointment is enclosed within a small groove cut into it ensuring complete contact of the ointment with the surface of the agar. The petri dishes are then incubated at 37°C for a period of 16 hours after which time the dishes are examined to determine the zone of inhibition of growth produced.

Much has been said in favour of the importance of the base, more particularly in favour of oil-in-water type of bases. But it must also be pointed out that the drug itself which is being incorporated plays a greater part in the healing of wounds than the advantages realised by a good base. Two per cent phenol in a variety of bases was not bacteriostatic but halogen derivatives of O-phenyl phenol in concentration as low as 1 per cent in the same base, had a marked bacteriostatic action.

### Absorption Through Skin

A review of the reports pertaining to the absorption of substances through the skin reveals a wide diversity of opinion, both as to the mechanism of absorption and the influence on absorption of the various substances used as ointment vehicles. Majority of the workers in this field holds the view that absorption takes place *via* the hair follicles, along the hair shafts and into the oil gland ducts.

According to Kionka, epidermis is a cellular membrane saturated with fats containing cholesterol and only substances soluble in these fats could diffuse through the epidermis. The base influenced the rate and degree of absorption.

Brown and Scott indicated that a substance must possess both oil and aqueous solubility in order to penetrate the human skin and that an extremely high or low partition co-efficient is less conducive to absorption than intermediate values. Sauerland also contended that the influence of the ointment base varies according to the substance. Starkenstein and Hendrych in 1936 attributed to cholesterol a penetrability regulating action and concluded that it must exercise a protective action. Bliss in 1934 and 1935 employing the histology of the skin to explain his conception of absorption, pointed out that the site of application, thinness of the skin, freedom from hair and richly supplied lymphatics were aids for absorption.

Here is an example of the diversity of opinion with regard to a very simple pharmaceutical preparation which is being used for thousands of years in different lands not without effect. Here is also an apparent dearth of clinical evidence or studies in comparison with the numerous *in vitro* studies. This is a great field for co-operative research between the pharmacist and the medical staff of various hospitals.

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## CASE NOTE

### PARALYSIS OF ABDOMINAL AND SPINAL MUSCLES IN POLIOMYELITIS

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Poliomyelitis can produce and leave behind bizarre paralysis. Any muscle of the body may be its unfortunate victim. In the distribution of paralysis leg muscles top the list. The trunk may be affected alone giving rise to spinal deformity, usually of a scoliotic or kyphoscoliotic type (Collier, Adie and Walshe, 1941). According to Agius, Bartolo, Coleiro and Seddon (1945), out of 426 cases of poliomyelitis in the epidemic at Malta (1942-3) the abdominal and spinal muscles were affected in 98 cases (23·0 per cent). But all had paralysis elsewhere as well. Only in 4 cases (0·93 per cent) of this series abdominal and

PHOTOGRAPH OF THE REPORTED CASE SHOWING WELLMARKED LEFTSIDED ABDOMINAL PROMINENCE AND SCOLIOSIS

spinal muscles were paralysed without any paralysis elsewhere. In an epidemic of acute anterior poliomyelitis among service personnel in Malta (1942-3), Bernstein, Clark and Tunbridge (1945) did not observe any case of paralysis of abdominal muscles although the trunk was involved alone in 2 cases and with others in 26 cases. In the New York epidemic of 1916, Lovett (1916) found no case of paralysis of abdominal and spinal muscles out of 1,166 cases.

Below is reported a case of poliomyelitis with paralysis only of abdominal and spinal muscles:

#### CASE REPORT

K.P.S., 3 years, Hindu male child, was admitted to the Children's Ward with the complaint of difficulty in walking, duration 2 months. The onset was after a stormy febrile attack.

*On examination*—Fairly nourished. Temperature, pulse and respiration rates normal. Well-marked left-sided abdominal prominence and scoliosis present. No tenderness of spine. Abdominal reflex absent in left upper and lower quadrants. No other abnormality detected anywhere or in any other system.

*Investigations*—Blood W. R. negative. X-ray of spine revealed no abnormality. Urine and stool normal.

*Acknowledgments*—My thanks are due to Major-General H. C. Buckley, M.D., F.R.C.S., C.S.I., I.M.S., Principal, Medical College, Agra for his kind permission to publish the report of the case.

I wish to express my appreciation of the services of my house-physician Dr. B. P. Kacker.

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(*Concluded from page 86*)

"Do not stir air into food while cooking.

Do not put them through a sieve while hot.

Do not use soda in cooking green vegetables.

In boiling foods, raise the temperature to the boiling point as rapidly as possible. Use as little water as possible.

Do not use long cooking processes like stewing when shorter methods are feasible.

Do not throw away the water in which vegetables have been cooked; use it in making gravies, sauces and soups.

Do not fry food valuable for their contents of vitamin A, D, and E.

Prepare chopped fruits and vegetable salads just before serving.

Start cooking frozen fruits while they are still frozen.

Serve raw frozen fruits immediately after thawing."

We as medical men can help the province by carrying out diet and nutritional surveys in different parts of the province. We can keep the public and Government informed about the food situation and the incidence of deficiency diseases.

We must educate the public regarding the right type of dietary habits and diets, proper ways of cooking and processing food-stuffs, because knowledge unapplied is little better than ignorance.

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JOURNAL OF THE

INDIAN MEDICAL ASSOCIATION

CALCUTTA, DECEMBER, 1946

## PROHIBITION OF OPIUM IN ASSAM

It is understood that the Government of Assam have decided to introduce in the coming budget session of the Assembly a bill called the Assam Opium Prohibition Bill 1947. The bill prohibits consumption (except for medicinal purposes) and smuggling of opium and aims to secure greater and more efficient control over smuggling and consumption of opium with a view to eradicate the evil of addiction. It is gratifying to note that Assam has again started this pioneer work once launched by her in April 1939.

Opium addiction is not uncommon in India. It is estimated that there are roughly 1 to 1½ million persons in British India (excluding Indian States) who habitually take this drug. This figure is arrived at on the calculation of 10 grains as the daily average dose on the total official consumption of opium and does not take into account the large quantity of smuggled opium. The League of Nations' standard for purely medical and scientific needs is 6 seers or 12 lbs. per 10,000 of population per annum. Chopra[1] gives an illuminating figure of the provinces in India. According to him the consumption per 10,000 of population per annum including medical and scientific need is as follows: Bengal—8 seers, Madras—8 seers, Punjab—12 seers, Bombay—10·05 seers, Central Provinces and Berar—9 seers, United Provinces—4 seers, Assam—19 seers. In Assam the figures for subdivisions are: Sadiya Frontier Tract—94 seers, Lakshmipur—70 seers, Sibsagar—45 seers, Nowgong —27 seers, Darrang—22 seers, Kamrup—8·9 seers. As early as 1910-11, the total consumption of opium for Assam stood at 1,568 maunds as against 12,527 maunds for the whole of India. Assam thus constitutes the worst province of opium addiction in India. In Assam and the Central Provinces opium smoking is as common as opium eating, the latter being the usual practice for the rest of India.

We drew attention[2] of the medical profession to this pioneer work of Assam in 1939. It is worthwhile to recall the scheme which was worked by the Government of Assam under the direction of Col. R. N. Chopra. Total prohibition of opium was introduced in two subdivisions *viz.,* Sibsagar and Dibrugarh to begin with from 15th April, 1939, and it was decided to accelerate the reduction of rations in other places, whatever the age of the addict, by deducting one-eighth each quarter, so that all issues by Government of raw opium would have completely come to a finish within two years. The whole of the scheme contemplated activities in three different ways. Firstly, an organisation of local committees and volunteers in different centres whose main object was (1) to carry on the propaganda, (2) to bring such addicts as would not willingly come for treatment, (3) to keep an eye on the addicts falling a prey again to the habit through the activities of smugglers. About 50 centres were opened for the treatment of addicts. The medicines given were mainly lecithin and glucose according to the schedule of Chopra (*loc. cit*). About 8,000 addicts were treated without a single fatality. The reports indicate that 70 per cent of addicts gave up opium. It is a pity that such a noble work could not be carried out to a finish due to various reasons.

In our country opium is sold to any and every person from government license shops between sunrise and sunset. While sale of opium is restricted from dispensaries and cannot be served except on prescriptions of a qualified medical practitioner, one can buy almost any amount of raw opium from the shops next door, such a contradiction of law is only possible in this country.

The Government of Assam will have the moral and medical support in their effort to eradicate this evil. It is time that the other provinces take up the work in their own sphere where opium consumption is high *e.g.,* Calcutta Town and Hooghly district in Bengal, East and West Godavari in Madras, Firozepore district, Lahore, Ludhiana and Amritsar in the Punjab, Amraoti, Akola and Balaghat in Central Provinces and Berar, the districts of Cawnpore, Benares and Lucknow in United Provinces. We hope in near future opium habit will be a thing of the past.

[1] Chopra, R. N.—*Indian M. Gaz.,* **70**: 122, 1935.
[2] Editorial—*J. Indian M. A.,* **8**:653, 1939.

## PENICILLIN AND DIPHTHERIA

Of the numerous bacilli that are sensitive to penicillin, *Mycobacterium diphtheria* is one. Still, very little work has been done to exploit the position in spite of the fact that antitoxins are bulky, difficult to get and prohibitive in cost. We, therefore, welcome an article by Prof. De and his colleagues[1] on the subject. As Dr. Ganguly, one of the associates, was a resident, they could plan such a daring investigation, as a constant watch is the key-note of their research. Ercoli, Lewis and Moench[2] reported the results of experiments where they showed that the growth of the bacilli *in vitro* is inhibited by penicillin in concentration of just over 1 unit per ml. This result when translated into actual cases should induce one to make more use of penicillin in diphtheria than at present. Unfortunately, animal experimentations as reported by an Editor[3] show that while penicillin prevents or cures experimentally produced bacteriæmia it fails completely to protect a guinea-pig with a subcutaneous lesion. Hence he opines that "it (penicillin) would have no appreciable value for the treatment of patients with established diphtheria." Prof. De's work now proves that the statement cannot be wholly taken as true. The value of his work lies in the fact that if penicillin is combined with antitoxin a much lesser amount of antitoxin will be required and the period of convalescence will be much shortened.

[1] De, Chatterjee & Ganguli—*J. Indian M. A.,* **16**:73, 1946
[2] Ercoli, Lewis & Moench—*J. Pharmacol,* **84**:120, 1945.
[3] Editorial—*Brit. M. J.,* **1**:656, 1946.

## CURRENT TOPICS

### THE WORLD'S FOOD:

### Subsistence and Maintenance Levels

A preparatory committee of the Food and Agriculture Organisation of the United Nations reported to the director-general (Sir John Orr, F.R.S.) on the nutritional aspect of the problems which came before the special meetings of the F.A.O. from May 20 to 27. The chairman was Dr. A. Hughes Bryan (UNRRA, Washington), and the members were Dr. John Cassels (U. S. Department of Commerce), Dr. L. A. Maynard (combined working party on European food-supplies 1944-45), Dr. A. P. Meiklejohn (UNRRA, London), Dr. E. P. Phipard (U. S. Department of Agriculture), Dr. W. H. Sebrell (National Institute of Health, Bethesda, Maryland), Dr. J. B. Youmans (consultant on Nutrition to Surgeon-General, U. S. Army), Dr. W. R. Aykroyd (F.A.O.), and Mr. D. Lubbock (F.A.O.).

The committee's report recognises:

1. *An emergency subsistence food-consumption level,* needed to preevnt the most serious undernutrition leading to disease and the danger of civil unrest. For European countries this level is defined as an average daily intake per head of 1900 calories, requiring a national average supply of not less than 2200 calories at the retail level.

2. *A temporary maintenance level* sufficiently high to maintain populations in fairly good health, but not for rapid and complete recovery. For European countries this level is defined as an average daily intake per head of 2200 calories requiring a national average supply of not less than 2500 calories at the retail level.

The committee regretted the need for considering these levels of consumption but felt that recommendations regarding them would be of practical value in the emergency.

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#### Emergency Subsistence

Table I gives the individual calories intake in the different age and sex-groups and various categories to workers at this level of consumption. It refers to European workers and indicates the point below which the consumption of no section of the population should fall if serious consequences are to be avoided. The figures are approximately 75% of those given in "recommended allowance" of the National Research Council, U.S.A., and the table is supported by actual experience of the point at which severe undernutrition becomes apparent among European populations.

Table I—Emergency Subsistence Calories Intake

| *Category* | *Calories per day* |
|---|---|
| 0—2 years | 1000 |
| 3—5 „ | 1250 |
| 6—9 „ | 1500 |
| 10—17 „ | 2000 |
| Pregnant and nursing women | 2000 |
| Normal consumers (sedentary) | male 1900 |
| | female 1600 |
| Moderate workers | 2000 |
| Heavy workers | 2500 |
| Very heavy workers | 3000 |

These figures refer to the actual intake of calories, and assuming a population which as regards age, sex, and activities is approximately the same as that of the United States the average intake is about 1900. It is important that the relation of per caput calorie intake figure of this nature to the actual food position in any given country should be clearly understood. Estimates of the total food-supplies available in a country are normally made at the retail level; that is to say, an allowance is made for the loss of food between source and the retail or market level. Allowances for loss up to this stage should equally be made in the case of food allocations to deficit countries.

A number of other factors must also be taken into consideration to ensure that no section of a population has a calorie intake below the emergency subsistence level. These are household waste (where food is short about 3% is wasted), and the extent to which distribution is equitable—which covers the proportion of farm to non-farm population, the access of urban populations to food--producing areas, the extent of black markets, the relation of the economic position of the poorer section of the population to food prices, and the age-distribution of the population and the categories of workers included in urban groups. Allowing for all these factors it is necessary, in order to ensure that all sections of a given population obtain the emergency subsistence minimum of 1900, that the per-caput calorie figure obtained by dividing the total food-supplies by the number of the population should be at least 300 calories in excess of the minimum. The committee point out that if the calorie intake of any section of the population falls below the emergency subsistence level for any length of time, then preparations must be made, in advance, for famine relief measure such as the provision of soup-kitchens, medical supplies, and hospital accommodation to deal with the disease which follows semistarvation. It is too late to organise effective relief once famine has made its appearance.

#### Temporary Maintenance

The minimum calorie intake per head per day is 2200, and the amount supplied should therefore be 2500 calories at the retail level. Table II shows how the figure of 2200 calories is arrived at.

At this level of diet special attention is given to the protein intake. The per-caput figure amounts to 60 grammes of protein daily, of which 10% should be in the form of animal protein. The committee state that an increase of protein intake will hasten the speed of recovery and that a "reasonably adequate" consumption of animal protein is a value for psychological reasons.

Table II—Temporary Maintenance Calories Intake

| *Category* | *Calories per day* | *Protein per day* |
|---|---|---|
| 0—2 years | 1000 | 30 |
| 3—5 „ | 1550 | 45 |
| 6—9 „ | 1750 | 55 |
| 10—17 „ | 2500 | 65 |
| Pregnant and nursing women | 2500 | 90 |
| Normal consumers (sedentary) | male 2200 | 65 |
| | female 1800 | 65 |
| Moderately heavy workers | 2500 | 65 |
| Heavy workers | 3000 | 65 |
| Very heavy workers | 3500 | 65 |

### Non-European Countries

The committee point out that in general non-European populations are of smaller average size than European populations, and that in warm climates their basal metabolism and energy output may be lower. Their habitual calorie intake is smaller than that of Europeans, and the emergency subsistence and temporary maintenance figures may generally be 15-20% below those in Tables I and II. Protein, in the committee's view, should be reduced by 10% only, but the recommendation about animal protein would "be unrealistic," as such populations normally consume little or none. Considerations regarding the relation between actual intake of food and the amount supplied at the retail level will in general apply equally.

### Other Questions

*Distribution*—The committee draw special attention to the need for beter distribution of food within countries, and point out that this involves effective and equitable crop collection, price control, the discouragement of black markets, and the application of ration scales based on the physiological needs of the different age, sex, and occupation categories within the population.

Governments responsible for seeing that food reaches those most in need of it must give an accurate picture of their food situation, and their method and efficiency of distribution are important.

*Milk*—The committee emphasise the value of processed milk in improving the nutrition of severely malnourished people. The following minimum quantities of milk are recommended for two priority classes:

| *Category* | *Milk allowances proposed Litres* |
|---|---|
| 0-2 years .. .. | 0·75 (whole mjlk) |
| 3-5 „ .. .. | 0·50 (whole milk) |
| 6-9 „ .. .. | 0·25 (whole or skimmed) |
| 10-17 „ .. .. | 0·50 (whole or skimmed) |
| Pregnant and nursing mothers .. | 0·50 (whole milk) |

The milk used may be either liquid milk or (if this is not to be had) evaporated or dried milk. And the committee specially recommend that in countries with a well-developed dairy industry an intensive effort should be made to produce dried skimmed milk in maximum quantities for distribution to countries in need. They believe that food imports into any country may be restricted in 1946 and 1947 and recommend that non-farm populations should be encouraged to cultivate vegetables for their own use and that plots of land and seed should be provided. They add that the consumption of vitamins A and C has been meagre in many urban areas of Europe during the winter and spring of 1946.

*Vitamins*—Special categories of the population—pregnant and nursing mothers, infants and young children—may benefit by receiving vitamins on medical direction. But the committee disapprove of indiscriminate distribution of vitamins as being likely to produce a false sense of security when the real need is for calories provided by food—*Lancet*, 1:971, 1946.

## VITAMIN DEFICIENCIES: STIGMAS, SYMPTOMS AND THERAPY

*This is an outline of the changes in the body resulting from vitamin deficiencies and their effective treatment. This material has been prepared by the Council on Foods and Nutrition in conjunction with medical nutritionists familiar with the clinical detection of vitamin deficiency. The signs and symptoms given in the outline represent current authoritative opinion as regards the stigma of vitamin lack. As stated in the introductory comment, present knowledge does not justify the characterization of many of these changes as conclusive or pathognomonic, particularly when observed as an isolated finding. Rather the abnormal finding should be considered as suggestive of the presence of a deficiency the existence of which should be corroborated by the finding of other changes and a history of dietary inadequacy.*

### Stigmas Suggesting Deficiency of Vitamin A.

*Xerosis of the conjunctiva:*

Thickening with loss of transparency, so that only the more superficial vessels of the bulbar conjunctiva are clearly seen, associated with more or less yellow pigmentation, especially along the horizontal meridian of the eyeball: infrequently associated with small foam-like plaques called Bitot's spots.

*Papular eruptions of pilosebaceous follicles:*

A crater-like feel, which in early stage resembles gooseflesh but, when more fully developed, presents the picture of keratosis pilaris. The extensor surfaces of the arms and thighs and the flexor surfaces of the legs are primarily affected.

*Xerosis or asteatosis of the skin:*

Dryness, scaliness and crinkling, in extreme cases resembling alligator skin. In early stages the condition is associated with keratosis pilaris but it persists and extends after follicles have disappeared, the body hairs being broken and later lost. All parts of the body are involved, but the skin of the extremities, particularly of the legs, is more severely affected than the skin of the head and the trunk.

*Follicular conjunctivitis:*

Hypertrophy of the follicles, particularly of the lower eyelids.

*Night blindness:*

Conspicuous only in cases of advanced, severe deficiency.

*Keratomalacia:*

Thickening with subsequent ulceration and necrosis of the cornea: present only in most severe and advanced forms of deficiency.

### Treatment of Vitamin A Deficiency

*Early deficiency state:*
25,000 U.S.P. units of vitamin A twice daily for two months or longer.

*More chronic states:*
25,000 U.S.P. units of vitamin A two to three times daily for a prolonged period.

### Stigmas Suggesting Deficiency of Thiamine

*Loss of strength* of the quadriceps: disproportionate to loss of general strength, evidenced by difficulty in rising from the squatting position.

*Loss of vibration sense:* first of the toes and later of the malleoli and tibias.

### Treatment of Thiamine Deficiency

*Acute deficiency state:*
10 to 20 mg. or more of thiamine twice daily until relief of symptoms; this may be days or weeks.

*Tenderness of the calves and hyperesthesia of the feet:*

*Diminution and loss of the achilles tendon and patellar reflexes first.* Other tendon reflexes are lost in the later stages of the polyneuritis of "dry beriberi".

*Edema* of the shins, ankles and knee joints: found in "wet beriberi".

*Enlarged heart with dependent edema* and elevated venous pressure: Poor response to rest and administration of digitalis unless thiamine is given. This is a late manifestation of severe deficiency (beriberi heart).

*Papillary edema with retinal hemorrhages:* associated with ophthalmoplegia and polyneuritis. The condition is a late manifestation of severe deficiency.

STIGMAS SUGGESTING DEFICIENCY OF RIBOFLAVIN

*Congestion of the limbic plexus:*

Visible with a small hand lens or the +20 lens of the ophthalmoscope; invasion of the cornea by capillaries arising from this plexus (vascularization) requires a biomicroscope and slit lamp for dectection.

*Cheilosis:*

Represented in chronic deficiency by excessive and irregular wrinkling, in acute deficiency by swelling and erasure of the normal wrinkling of the lips. Reddening, thinning, scaling, chapping of epithelium are associated.

*Angular stomatitis:*

Various combinations of erythema and open fissuring in the angles of the mouth with or without a white, moist maceration (perleche); scars of healed fissures.

*Dyssebacia:*

An erythema overlaid with somewhat greasy, flaky accumulations resembling hoar frost, noted mostly in the alae nasi, canthi, pinnae and other folds of the skin, accompanied in some cases by coarsening and elevation of the sebaceous follicles of the nose and cheeks, the latter also seen with deficiency of vitamin A.

*Magenta tongue:*

A purplish red coloring with moderate edema and flattening of filiform papillae; observed in more advanced deficiency.

STIGMAS SUGGESTING DEFICIENCY OF NIACIN

*Edema of the tongue:*

Shown by dental indentations.

*Increased redness of the tongue:*

Beefy red in chronic states; scarlet in severe acute deficiency.

TREATMENT OF RIBOFLAVIN DEFICIENCY

*Acute deficiency state:*

5 mg. of riboflavin three times daily for weeks.

*Chronic deficiency state:*

3 to 5 mg. of riboflavin three times daily for a prolonged period.

TREATMENT OF NIACIN DEFICIENCY

*Acute deficiency state:*

100 mg. or more of niacinamide twice daily for weeks.

*Chronic deficiency state:*

5 to 10 mg. or more of thiamine twice daily for a prolonged period.

*Congestion and hypertrophy of the papillae of the tongue, followed by fusion and atrophy:*

In early stage the fungiform papillae are congested and hypertrophied. This is followed by hypertrophy of the filiform papillae and later by their flattening. As they atrophy they fuse or mat together with multiple fissuring to give a cobblestone appearance and finally baldness. Vincent's infection of tongue and fauces, ulceration and pseudomembrane formation may or may not accompany these changes in the more advanced stages of this deficiency.

*Dermatitis:*

Erythema, rough scaling, with ulceration and formation of bullae, affecting primarily areas of the skin exposed to light; namely, wrists, ankles, neck and face; observed only in severe deficiency (pellagra) and then frequently associated with diarrhœa and dementia.

*Encephalopathy:*

Clouding of consciousness, cogwheel rigidity and grasping, sucking relexes observed in acute severe deficiency.

STIGMAS SUGGESTING DEFICIENCY OF ASCORBIC ACID

*Redness, edema, tenderness and bleeding on pressure of the gums:*

Observed in acute or subacute deficiency of moderate severity, sometimes with, but usually without, other signs of ascorbic acid deficiency.

*Thickening and increased firmness of the gums:*

With recession and exposure of the base of the teeth, including recession of interdental papillae; observed in chronic deficiency.

*Retraction of the gums:*

Leaving pockets between gum and tooth, secondary infection and resulting pyorrhea; observed in chronic deficiency.

*Loosening and shedding of the teeth.*
*Increased capillary fragility:*

Manifested by petechial hemorrhages of the skin, especially in the tourniquet test; observed in more severe acute and subacute deficiency. Easy bruising, spontaneous ecchymosis of the skin, idiopathic hemorrhage into joints and slow healing of wounds, observed in severe acute and subacute deficiency.

STIGMAS SUGGESTING DEFICIENCY OF VITAMIN D

*Deformities of the skeleton:*

Bowed legs, malformation of the chest (funnel breast) and defects of the teeth may be residues of early rickets which is usually no longer active or susceptible to treatment; enlargement of the wrists, elbows, knees, ankles and costochondral junc-

(*Concluded at foot of page 106*)

TREATMENT OF ASCORBIC ACID DEFICIENCY

*Acute or subacute deficiency state:*

100 mg. or more of ascorbic acid for weeks.

*Chronic deficiency state:*

100 mg. of ascorbic acid three times daily over a prolonged period.

TREATMENT OF VITAMIN D DEFICIENCY

*In infants:*

1,500 to 2,500 U.S.P. units of vitamin D daily, continued for several months (double this amount for premature infants).

*Chronic state;*

100 mg. of niacinamide twice daily over a prolonged period.

# CURRENT MEDICAL LITERATURE

### Prognosis in Angina Pectoris

From the wealth of carefully documented clinical material in the Mayo Clinic, Willius and his colleagues (*J.A.M.A.*, **131**:95, 1946) have produced the most statistically satisfactory study so far published of the survival rate in angina pectoris. Their figures are based on 3440 cases seen at the clinic during the ten-year period 1927-36, all of them followed up for at least five years. The male: female ratio was 4·3:1. The average age of the patients at the time of onset of the angina was 57·1 year, 88 per cent falling in the age-group 40-69 years. Only 125 patients (3·6 per cent) were under 40, and 276 (8 per cent) were 70 years of age or older.

Only 10 per cent of the female cases were in the 40-50 age-group, whereas 55 per cent were in the age-group of 60 years and older, compared with 46 per cent of the men. This last observation fits in with the general impression that coronary disease manifests itself at a later age in women than in men. The highest mortality occurred during the first year after diagnosis, when the rate was 18 per cent. From year to year thereafter the mortality was fairly constant at about 10 per cent. Survival-rates were consistently higher for women than for men—thus at five years from the time of diagnosis the survival-rate was 71 per cent for women and 58 per cent for men, while at ten years the rates were 49 per cent and 33 per cent. The average five-years-survival rate for the entire series was 53 per cent. There was no evidence to support the general belief that angina pectoris in younger patients carries a relatively good prognosis.

The five-years-survival rate of patients who had no clinical or radiological evidence of cardiac enlargement was 62 per cent compared with 39 per cent for those with cardiac hypertrophy. Hypertension also exerted an adverse effect on prognosis, the five-year-survival rate for those without hypertension being 61 per cent compared with 46 per cent for those with hypertension. The prognostic value of ophthalmoscopic examination in hypertensive subjects was strikingly corroborated. Among the 499 patients classified as group I according to the state of the retinal vessels, the five-year-survival rate was 52 per cent., compared with 42 per cent for the 279 patients in group II and 16 per cent for the 55 in group III. Congestive heart-failure caused the five-year-survival rate to slump to 16 per cent, the corresponding figure for all cases of congestive failure, regardless of aetiology, being 30 per cent. Analysis showed that, used with discrimination, the electrocardiogram can be a help in prognosis. The five-year-survival rate for those with normal electrocardiograms was 70 per cent; for those with significant T-wave negativity, or Q-changes, or both, it was 43 per cent; and for those with conduction defects it was 35 per cent. The lowest five-year-survival rate of all (17·5 per cent) was in those with auricular fibrillation, but the smallness of the group (57) reduced the significance of this observation.

Thus assurance can be given to patients that prognosis of angina pectoris is not such a gloomy one after all. Five years from the time of diagnosis more than half the patients with angina pectoris will still be alive, while after ten years a third of the men and half the women will still remain—*Lancet*, **1**:894, 1946.

### Angina Pectoris and Tobacco

The term "tobacco angina" has been employed for many years; its importance lies in the concept that smoking tobacco may constrict the coronary arteries and thus adversely affect the heart. Recently Pickering and Sanderson (*Clinical Sc.*, **5**:275, 1945) studied several patients who developed cardiac pain of an anginal nature following smoking. One patient was subjected to many tests and careful studies without evidence being found that smoking produced coronary vasoconstriction; when the patient smoked before or during exercise, tolerance to exercise was not reduced. All the evidence, the authors say, was consistent with the view that smoking by this patient was a factor in producing anginal pain because it increased the work of the heart through the pulse rate and blood pressure. The use of tobacco, most cardiologists agree, is not the primary cause of coronary sclerosis, which is the pathologic lesion underlying angina pectoris. In the patient studied most completely, smoking produced anginal pain only in the period shortly after the disappearance of the pain produced by effort, and this occurred only if the pulse rate rose sufficiently. The investigators believe that their studies provide an alternate hypothesis to the theory that constriction of the coronary arteries by tobacco is the cause of anginal pain precipitated by smoking; namely, that tobacco acts in this respect only by its effect on increasing the work of the heart. The investigation further casts doubt on the usefulness of the term "tobacco angina"—*J.A.M.A.*, **131**:143, 1946.

### Influence of Digitalis on Blood Clotting

Decourt and Barbato (*J.A.M.A.*, **131**:353, 1946) of the department of Clinical Medicine of the University of Sao Paulo have reported their investigations on the influence of digitalis on the blood clotting time. They wished to ascertain the exact thromboplastic action of digitalis. Three groups were observed; the first, 16 cardiac patients with different functional capacities who received digitalis in therapeutic doses; the second, 16 normal persons, who received during three days 9 cat units of digitalis (3 units a day); the third, 4 cardiac patients treated without the use of digitalis (rest in bed, therapeutic dehydration and adequate diet). The determination of the blood clotting time has been done by the method of Lee-White. Determinations were made before the use of digitalis and then every fourth day during the time the drug was being administered to the patients.

In 15 out of 16 cardiac patients of the first group the clotting time showed a definite reduction: the average time of seven minutes and twenty-seven seconds (minimum four minutes, maximum eleven minutes), was reduced to five minutes and thirty seconds (minimum three and one-half minutes, maximum eight minutes). No relation was found between the degree of reduction of clotting time and the functional capacity of the heart or venous pressure. The reduction of the clotting time was present only during the use of digitalis and reverted to its previous value after the drug was discontinued. Comparable results were obtained in the second group of 16 normal persons. The third group of 4 cardiac patients who did not receive digitalis showed no change in the clotting time, in spite of rest, dehydration and reduction in the venous pressure.

The authors believe that the results strongly suggest a reduction of the blood clotting time with the use of digitalis, with possible significance as to embolism and thrombosis in cardiac patients. Although these accidents may occur in patients who are not taking digitalis, the results of the experimentation suggest a more careful use of the drug.

### Atabrine Sensitivity

Agress (*J.A.M.A.*, **131**:14, 1946) writes that in a large series of Chinese patients receiving atabrine for prophylaxis or treatment for malaria, 5 with severe hepatitis and exfoliative dermatitis were encountered, 3 of whom died of this complication. This represented a very small incidence, about 1 in 2,000 to 3,000 cases.

From clinical and pathologic studies it is concluded that atabrine was the causative agent of the hepatitis and the exfoliative dermatitis.

The reaction may occur from extreme sensitivity on as little as 0·1 gm. of the drug or may be a toxic reaction from prolonged and repeated administration.

Prompt recognition and treatment of these complications with recognized detoxifying agents like vitamin C and liver extract, intravenous glucose and plasma, combined with withdrawal of the drug may prove to be life saving procedures, although the mortality in 5 cases was 60 per cent.

The twenty-four hour patch atabrine test giving only 3 per cent false positive reactions with normal skins and 8·3 per cent false positive reactions in patients with existent dermatitis is a useful test for investigation of atabrine sensitivity.

### Diet in the Treatment of Infective Hepatitis

Wilson and others (*Lancet*, **1**:881, 1946) write that the administration of 5 gm. of cysteine daily by mouth to 52 patients with infective hepatitis produced a significant shortening of the period of recovery compared with 51 control cases. This appeared to be due to the smaller number of relapses in the treated group.

A comparison of the progress of 52 patients on a lowfat diet with that of 51 on a high-fat diet revealed no significant difference, in the rate of recovery.

### Proteolysed Liver Extract in the Treatment of Tropical Macrocytic Anaemia

Das Gupta and others (*Indian M. Gaz.*, **81**:122, 1946) write that the discovery of Monot and Murphy (1926) of the curative value of mammalian liver in pernicious anaemia led to investigations into the nature of substance or substances present in the liver which are responsible for its hæmopoietic activity.

The average composition of the different mammalian livers was determined and found to be as follows (Table I):—

Table 1—Average Composition of Mammalian Livers

| | *Moisture per cent* | *Total protein per cent* | *Fat per cent* | *Carbohydrate per cent* | *Mineral matter per cent* | *Iron mgm. per cent* |
|---|---|---|---|---|---|---|
| Buffalo .. .. | 69·42 | 20·08 | 2·75 | 6·22 | 1·53 | 23·78 |
| Cow .. .. | 72·58 | 16·85 | 5·14 | 4·00 | 1·50 | 30·00 |
| Sheep .. .. | 67·10 | 18·18 | 8·07 | 5·53 | 1·19 | 29·00 |
| Pig .. .. | 73·60 | 15·16 | 5·77 | 42·2 | 1·35 | 40·00 |

Proteolysed liver extracts were prepared both from the liver of sheep and cows. The different steps in the preparation are as follows:—

(*i*) *Collection, weighing and mincing*—Liver from healthy animals is collected from the slaughter-house in the evening immediately after the animal is killed and brought to the laboratory in container kept cool with ice. The extraneous matter, fat and fibrous tissues are removed mechanically as far as possible, the liver is weighed and then minced. It is next treated with about half its volume of distilled water, is thoroughly stirred and kept in the cold chamber overnight after adding 0·5 per cent chloroform as preservative.

(*ii*) *Digestion with papain*—Next morning powdered papain is added to the mixture in the proportion of 2 gm. of papain to every pound of minced liver and another volume of distilled water is added, so that the total volume of distilled water in c.cm. is equal to the weight of the minced liver in grammes. The digestion is done in an enamelled vessel at a temperature of 60°C. for 3 hours with occasional stirring. At the end of 3 hours, the temperature is raised to 100°C. and the mixture is allowed to boil vigorously for 5 to 10 minutes.

(*iii*) *Filtration*—The hot digested mixture is filtered through gauze and the filtrate is kept in the cold chamber with the addition of 0·5 per cent chloroform as preservative.

(*iv*) *Concentration under reduced pressure*—The filtrate is concentrated under reduced pressure at a temperature not exceeding 60°C. to about one-third of its volume. Alcohol (10 per cent) and glycerine (20 per cent) are added as prescribed in the B.P. 1932 for the preservation of Extractum Hepatis Liquidum. Each fluid ounce of the extract represents approximately 50 gm. of raw liver.

(*v*) *Analysis of the proteolysed extract*—A part of the fresh concentrate was dried to solid powder. The yield of dry solid matter was approximately 16 per cent of the weight of raw glands. It was analysed for its contents of total nitrogen, mineral matter and iron. The solid matter 13·302 per cent nitrogen (equivalent to 83·13 per cent protein), 4·8 per cent mineral matter consisting of 0·044 per cent iron; and that from bovine liver digest 12·15 per cent nitrogen (equivalent to 75·93 per cent protein).

The nature and proportions of the nitrogenous constituents were determined by fractional precipitations and by estimation of nitrogen by Kjeldahl, and aminonitrogen by van Slyke apparatus according to the methods of Schryver and Buston. The results of the analysis are shown in Table II.

Table II

| *Nitrogenous bodies from different liver digest* | *Meta-protein per cent* | *Proteoses (primary and secondary) per cent* | *Peptone per cent* | *Nitrogenous bodies containing amino-nitrogen (van Slyke) per cent* | *Nitrogenous bodies giving ammonia per cent* |
|---|---|---|---|---|---|
| Sheep liver .. | 3·68 | Traces | 50·30 | 38·55 | 7·47 |
| Bovine liver .. | Traces | 26·49 | 15·75 | 49·85 | 7·91 |

(*vi*) *Ripening, filtration and packing*—The mixture is kept for 2 to 3 weeks in cold chamber so that more unstable meta-proteins may precipitate out after being denatured. The mixture is then filtered through Seitz pads and the filtrate is usually found to be sterile. It is of light red-brown colour, of thin consistency with agreeable taste and odour. It is filled in sterilized ampoules, pulled out at both ends, in lots of 15 and 25 c.cm. and sealed. Kept in the cold chamber the extract keeps well for a long time.

As a hæmatinic, proteolysed liver extract was given to 15 cases of frankly macrocytic anæmia in the Carmichael Hospital for Tropical Diseases. Sheep's liver extract was used in 4 cases, bovine liver in 11.

The results obtained are very similar to those of Davis and Davidson, *viz.*, that the proteolysed liver is quite effective in small dosage in uncomplicated cases of tropical macrocytic anæmia with megaloblastic reaction of the marrow; complicated cases with 'dimorphic' erythropoiesis are less amenable to treatment and require much bigger dosage and longer period of treatment. These results indicate that the missing factor or factors in tropical macrocytic anaemia is present in proteolysed liver in appreciable amount. The total dosage required for the effective treatment even of an uncomplicated case would naturally vary, but extracts derived from 100 grammes of raw liver given for 10 to 20 days appear to be sufficient to bring the blood picture to normal in most cases. Oral administration of proteolysed liver is as effective as potent liver extracts given parenterally, thus simplifying the treatment not only of individual cases but also on a mass scale.

### Chronic Diarrhœa Treated with Folic Acid

Carruthers (*Lancet*, **1**:849, 1946) writes that 4 severe cases of hypochromic anæmia were selected for treatment with folic acid. The dosage was 40-60 mgm. daily, and all other therapy was suspended. In one of these patients the anæmia was secondary to chronic malaria, in another to chronic glomerular nephritis, and in the remaining two to chronic diarrhœa. The red-cell counts ranged from 560,000 to 1,800,000 per c.mm., and the hæmoglobin estimations (Sahli) from less than 10 per cent to 30 per cent, but in no case did treatment with folic acid in the 5-7 day period allowed lead to any noteworthy improvement in the anæmia. However, in the 2 cases with chronic diarrhœa an immediate and definite improvement in the stools took place, and this led the author to abandon the use of the limited supply of folic acid for the treatment of anæmia and to try its effects in 6 cases of chronic diarrhœa.

In these 6 cases of chronic diarrhœa, folic acid therapy restored the stools to normal or approximately so within 2-5 days. The absence of any common ætiology suggests that in any longstanding diarrhœa a nutritional factor prolongs the production of abnormal stools. Folic acid appears to correct this defect. Thus he concludes:

Folic acid had no effect on four severe cases of hypochromic anæmia. Folic acid produced rapid improvement in the character of the stools in 6 cases of chronic diarrhœa of varied ætiology, though it did not affect the anæmia present. A nutritional deficiency probably explains the persistence of the diarrhœa in these cases.

### Radioactive Iodine in Hyperthyroidism

Chapman and Evans (*J.A.M.A.*, **131**:86, 1946) write that in hyperthyroidism orally administered doses of radioactive iodine, carried in about 1 mgm. or less of ordinary iodine, are concentrated largely in the thyroid gland. The beta rays from the radioactive iodine deliver within the thyroid an internal radiation which is physically similar to rœntgen radiation. The radiation dose in a patient who swallowed 14 millicuries has been calculated as equivalent to approximately 3,490 rœntgens, due to the 12-hour isotope.

Between May 1943 and March 1945, 22 patients having hyperthyroidism were treated with large doses of radioactive iodine. No other form of therapy was given.

Fourteen patients responded well to a single dose or radioactive iodine; 3 were given two doses and 5 were given three doses. Myxœdema has followed this treatment in 4 patients. Two patients after treatment with this agent, though improved, still have mild hyperthyroidism.

Reactions which resembled rœntgen ray sickness were observed in 6 patients following large doses of radioactive iodine. Fibrosis of the thyroid has been observed in biopsy of 2 patients after treatment.

Patients who have not responded to other forms of treatment or have been sensitive to iodine or thiouracil have responded well to radioactive iodine. Ordinary iodine is not necessary with radioactive iodine treatment.

It is believed that therapy with radioactive iodine can be added to the growing list of medical methods for the control of thydrotoxicosis.

### Neostigmine in Spastic Paralysis from Cerebral Lesions

Kabat and Jones (*J. Nervous & Mental Dis.*, **103**:107, 1946 Ref. *J.A.M.A.*, **131**:359, 1946) review the results obtained with neostigmine in 32 cases of chronic spastic paralysis or related conditions from cerebral lesions. Intramuscular injections were given six times a week. The dosage varied from neostigmine methylsulphate 1 c.c. of 1:2,000 solution (0·5 mg.) with atropine sulphate 1/200 grain (0·32 mgm.) to neostigmine methylsulphate 3 c.c. of 1:2,000 solution (1·5 mgm.) with atropine sulphate 1/100 grain (0·65 mgm.). In a few cases neostigmine bromide was given orally to supplement the injections in a dosage of 15 mgm. three times a day to 45 mgm. of neostigmine bromide with atropine sulphate 1/150 grain (0·5 mgm.) three times a day. Neostigmine was administered after meals to diminish toxic effects. It has been administered to 11 patients who had developed hemiplegia from one to thirty-one years before. Improvement was observed in all and was retained after therapy was discontinued. Eight patients who had had hemiplegia for months were treated with neostigmine, and accelerated recovery of motor function was observed in some. Of 6 patients with the spastic type of cerebral palsy who were given neostigmine 3 children all showed significant improvement, while of 3 adults only 1 showed slight improvement. Three patients with the athetoid type of cerebral palsy all showed significant improvement from neostigmine therapy. Two children with mild ataxia, 1 of whom had cerebral palsy with severe stuttering and the other of whom had had a subarachnoid hæmorrhage at the age of 1-½ years, improved greatly on neostigmine. Definite improvement from neostigmine occurred in ataxia and facial paralysis in a patient who had had an accoustic neuroma removed more than three years before. Moderate improvement was observed in a disability of the upper extremity in a patient who had had a prolapsed cervical disk removed. One patient with pseudohypertrophic muscular dystrophy derived no benefit from neostigmine. Three patients with lesions of the spinal cord obtained slight

or no improvement. Neostigmine decreases spasticity, thereby decreasing resistance to passive motion, increasing range of joint motion, relieving muscular pain and decreasing deformity. It facilitates voluntary motion, resulting in restoration of motions which had long been absent, increasing strength, improving coordination and diminishing fatigue. In addition, neostigmine has resulted in improvement in athetosis, ataxia, dysphagia, dysarthria, facial paralysis, motor aphasia and conscious proprioception from a variety of types of lesion of the brain. Improvement has been retained after therapy was discontinued. For maximal functional recovery, neostigmine therapy should be accompanied by exercise and muscle training. Evidence is presented that the locus of the therapeutic action of neostigmine in these cases is on the central nervous system.

### Specific Treatment of Acute Nephritis

Acute nephritis is often associated with a focal infection, especially of the upper respiratory tract, so the advent of chemotherapy was expected to provide a valuable weapon in the control of this disease. Early reports tended to be over-enthusiastic, and Rapoport, Rubin, and Waltz (*Am. J. Med. Sc.*, **211**:307, 1946) have provided a valuable corrective in their careful study of 33 children with acute glomerulonephritis treated with sulphanilamide and compared with a control group of 40 children treated similarly in all other respects. The original sulphanilamide was used first because the study was begun in 1938, when this was the drug of choice, and subsequently because of the possibility of renal complications with the later preparations. In the assessment of results particular attention was paid to the Addi's urinary sediment counts. All the children in both groups recovered completely from their renal disease, and there was no significant difference in the duration of the renal inflammatory process or of the disturbed renal and cardiovascular functions in the two groups. The sulphanilamide had no demonstrable deleterious effect on the kidneys. The dosage was 1 grain per pound body-weight daily for five days, following an initial dose of half the calculated total daily dose; then a continuation course of half the standard dosage for a further fifteen days; and finally a maintenance dose of gr. 10-20 daily for a variable period of two to six weeks. Blood examination showed an adequate concentration. Despite the apparently negative results, Rapoport and colleagues urge that the treatment of infections in patients with nephritis by means of sulphonamides is rational therapy.

The disadvantages of sulphonamide therapy are partly overcome by using penicillin, which has no toxic actions on the kidney. Moncrieff (*Lancet*, **2**:706, 1946) advocated the use of this drug in acute nephritis two years ago and doubtless it has often been employed since then. Sen (*Am. J. Med. Sc.*, **211**: 289, 1946) has lately reported 12 cases from India, all children with severe acute nephritis. Using a solution containing 10,000 units per c.cm., he gave injections of 5000-10,000 units three-hourly or four-hourly, with a total dosage ranging from 192,000 to 640,000 units over a period of three to eight days. Of the 12 cases, which were chosen for their severity, 8 made a complete recovery, 1 died, and 3 are classified as "doubtful" or "satisfactory" because abnormal constituents still remained in the urine at the time of the report. It is interesting to compare these results with the American series treated with sulphanilamide in which all the children, treated and controls, recovered completely, and also with the figures given by Ellis (*Lancet*, **1**:1, 34 & 272, 1942) for his 225 cases of type 1 nephritis. Here the recovery-rate was 82 per cent, with death in the acute stage in 4 per cent, a rapid progressive course in 4 per cent, and a slowly progressive course—albuminuria persisting as in Sen's "doubtful" cases—in 10 per cent. Ellis collected his cases before chemotherapy was introduced, and it seems fair to conclude that the new weapons have made no difference to the outlook in acute nephritis, except that a focus of infection can be more readily eliminated—*Lancet*, **1**:892, 1946.

### Treatment of Agranulocytosis

"Death in agranulocytosis," says Dameshek (Leukopenia and Agranulocytosis, Oxford, 1942) "probably is not due to the lack of granulocytes as such but to the bacteremia and septicemia which inevitably ensue. The period during which the blood and tissues are depleted of granulocytes is a critical one. It is during this time that generalised sepsis may occur. The patient thus may die of sepsis during spontaneous bone-marrow recovery." There is, however, no very clear evidence that such sepsis does occur in agranulocytosis; on the contrary, the local lesions are often astonishingly free from pathogens, and a positive blood-culture is rare. Dameshek treated agranulocytosis with sulphonamides, which, in view of their known propensity for causing the disease, was perhaps not a very happy choice. Penicillin seemed to be the answer, since it does not depress granulopoiesis, and there have now been several enthusiastic reports of its value but in spite of their acceptance of the sepsis theory, few workers have been willing to place their trust in penicillin alone. Thus Sprague and Ferguson (*U. S. Nav. Med. Bull.*, **43**:1014, 1944) had a case of sulphonamide agranulocytosis with massive abscesses; penicillin was given and was credited with the recovery, but the patient also had blood-transfusions, pentose nucleotide, yellow bone-marrow, and liver intramuscularly. Smith, Cohen, and Nichols (*J.A.M.A.*, **126**:1927, 1944) had 2 cases following mapharsen, and Boland, Headley, and Hench (*J.A.M.A.*, **130**: 556, 1946) a case following gold therapy for rheumatoid arthritis; all these patients received multiple treatment. Even Dameshek and Knowlton (*Bull. New Eng. Med. Centre*, **7**:142, 1945) treated a case of sulphonamide agranulocytosis with transfusion as well as penicillin; and there are other similar reports of multiple treatment in which the credit is given to penicillin for no better reason, it seems, than that it is the latest on the list.

Tyson, Vogel, and Rosenthal (*Blood*, **1**:53, 1946) report a more careful study. They had 9 cases of thiouracil agranulocytosis, of which 4 were fatal and 5 recovered. The only positive blood-culture occurred in the fatal group, the organism being a somewhat resistant *Streptococcus viridans*. Of their recovered cases, 3 had blood-transfusion and liver extract, but no pentose nucleotide, as well as penicillin; but 2 actually had only penicillin in relatively small amounts of 10,000—15,000 units 3-hourly. The evidence for the value of penicillin in agranulocytosis is thus not very convincing and already the next "newest" rival has appeared. Cantor and Scott (*Canad. M. A. J.*, **52**:368, 1945) report good results with pyridoxine, a member of the vitamin-B complex: the hydrochloride was given intravenously in doses of 125-200 mgm. daily to 3 cases, but 2 of these had also received blood-transfusion.

Clearly no specific for agranulocytosis has yet been found. The search is likely to be difficult with a disease that, despite all the new methods of producing it—sulphonamides, thiouracil, gold and the like—is still far from common, and whose course is either death or rapid spontaneous recovery. It would be a brave man who would withold transfusion or pentose nucleotide

in a case that is not doing well, since these are the only two measures which are of value, however slight. But if sepsis is present, penicillin has its place as an antibacterial drug without depressant effect on the formation of granulocytes—*Lancet*, 1:894, 1946.

### Headache Treated with Intravenous Sodium Nicotinate

Goldzieher and Popkin (*J.A.M.A.*, **131**:103, 1946) write that the effect of intravenous sodium nicotinate was studied in 100 consecutive patients with severe headache. Seventy-five were completely relieved. The intravenous route was chosen for precision and the decisiveness of the clinical effect; 100 mgm. of nicotinic acid or its equivalent as the sodium salt was taken as the standard dose because this amount was found adequate to produce a flush in almost every case.

The relief of headache appears to be correlated with the degree of peripheral flush.

Intravenous sodium nicotinate is recommended in the symptomatic treatment of (*a*) severe idiopathic headache. (*b*) migraine and (*c*) postspinal tap cephalalgia.

### Surgical Complications of Ascariasis

Milwidsky (*Acta Med. Orient.*, **4**:370, 1945 Ref. *J.A.M.A.*, **131**:74, 1946) gives the following reports on the surgical complications to which ascariasis may give rise. Discussing ileus due to ascaris, he reviews 10 cases of his own and shows that there are five different types: (1) mechanical obstruction by worm convolutes, (2) a paralytic type of ileus, (3) a spastic ileus, (4) invagination by ascariasis and (5) volvulus by ascariasis. The author has observed perforations of the bowel, postoperative disturbances due to ascaris, appendicitis and diverticulitis as well as ascariasis of the stomach and duodenum, bile ducts and liver. The 17 cases mentioned in this paper were encountered in the course of six years. The most effective method to forestall surgical complications of ascariasis is its prevention by a antiparasitic prophylaxis and early anthelmintic treatment if an infestation has taken place. As soon as the acute abdominal symptoms appear, anthelmintic treatment may be dangerous. At that stage surgical intervention becomes imperative.

### Pain of Organic Disease Relieved by Partial Lobotomy

Freeman and Watts (*Lancet*, 1:953, 1946) in reporting five cases in which prefrontal lobotomy was performed for the relief of pain which had proved refractory to other methods of treatment observe that in all cases the pains were severe, constant, and disabling, and there was a considerable structural basis for them yet the emotional component, the emotional response to the pain, seemed to be more disabling than the pain itself.

Previous observations had indicated that, when unbearable pain (psychalgia) is one of many symptoms of a mental disorder, prefrontal lobotomy relieves the pain along with the nervous tension and other emotional manifestations.

The present cases indicate that, when pain due to organic disease becomes unbearable and the fear of pain becomes as dreadful as the pain itself, prefrontal lobotomy is a desirable procedure.

Psychosurgery alters the subject's reaction to pain without materially changing his ability to feel pain. Pain may be present but when divorced from its implications—insecurity, disability, guilt, death—it then becomes bearable and may be accepted with fortitude.

### Osteomyelitis of the Spine

Pyogenic osteomyelitis of the spine often presents a baffling problem in differential diagnosis; its manifestations may be deceptively mild or they may be referred to remote parts of the body. Guri (*J. Bone Jt. Surg.*, **28**:29, 1946) who has investigated the problems of localisation and diagnosis of the infective process, points out that this may present as several different syndromes. There may be acute pain around the hip-joint with flexion spasm and fever, simulating a suppurative or tuberculous arthritis; but movements other than extension are not restricted, and local spinal tenderness and spasm can be elicited if sought for. The abdominal syndrome, with pain, hyperaesthesia, and leucocytosis, may mimic appendicitis, and appendicectomy has been performed. Another group of cases is marked by meningeal irritation, with malaise, headache, and meningism, very much as in an acute or tuberculous meningitis; since the cerebrospinal fluid may exhibit a reactive pleocytosis, the final diagnosis rests on the often delayed appearance or radiographic foci. Most cases do present with back pain, though in less than half is it really acute, with severe tenderness and spasm, fever, and toxaemia. It must be remembered that the condition is sometimes complicated by an epidural abscess; when this develops slowly after a mild onset and causes paraplegia it may be mistaken for a neoplasm of the cord.

When osteomyelitis is insidious in onset, as it often is diagnosis from other conditions such as typhoid and pneumococcal spondylitis, or brucellosis, is usually settled by the history and by agglutination and skin tests; but the differentiation from tubercle may be extraordinarily difficult. If the lesion is localised in the neural arches it is practically always of pyogenic origin; tubercle in this site is rare. Apart from culture of pus from the abscesses—which resemble cold abscesses or the discovery of osteomyelitic foci elsewhere in the skeleton, diagnosis usually depends on serial radiography. The x-ray appearances are various. There may be a localised focus in a vertebral body or the process may be closely related to an intervertebral disk, Indeed, it has been suggested that some cases are primary infections of the disk with narrowing and collapse; and there are numerous reports of disk degeneration and low-grade regional osteomyelitis of the spine following lumbar puncture. In other cases the front and sides of the vertebral body or the epiphyseal ring are involved.

Neither the shape of the lesion nor its localisation, but only its radiographic evolution over a considerable time, establishes it as non-tuberculous. Pyogenic spondylitis is often a diffuse process without localisation, leading to a dense reactive selerosis which bridges the vertebral bodies. Of course such sclerosis is rarely observed in tuberculosis; but it is of interest that radiography of postmortem specimens in Pott's disease does often reveal patchy sclerosis and sequestration which cannot be observed in the living—*Lancet*, 1:787, 1946.

### Poliomyelitis Complicating Pregnancy

Waaler (*Acta. Med. Scandinavia*, **123**:209, 1946 Ref. *J.A.M.A.*, **131**:492, 1946) reports 8 cases of poliomyelitis in pregnant women between 18 and 38 years of age. Seven cases occurred during an epidemic in Bergen, Norway, in 1941; the eighth case occurred in 1944. There were two fatalities. The author observed that poliomyelitis is not more severe in

pregnant women except during the last months of pregnancy, when there may be great discomfort if the respiratory muscles are involved. The prognosis is probably worse for the mother in late pregnancy. The disease has little influence on pregnancy and labour. Labour is usually normal, and Cesarean section is indicated only when paralysis embarrasses the respiration or when genitourinary complications are serious. It seems likely that poliomyelitis is more frequent in pregnant women than in other adults, and the cases hitherto observed have been uniformly distributed among the various stages of pregnancy. No evidence has been produced of intrauterine transmission of poliomyelitis. Of this series 5 new born infants did not show any sign of paralysis or malformation. Follow-up investigation of age showed that all children were well and that they had learned to walk at the usual age. In 1 case of stillbirth with spontaneous labour there was a history of previous stillbirth and no evidence that poliomyelitis was responsible. Microscopic examination of the nervous system of the fœtuses of the 2 mothers who died in the sixth and eighth month respectively of pregnancy did not reveal any abnormality.

### Ammonium Chloride in Prevention of Diethylstilbestrol Nausea

Hudgins (*West Virginia M. J.*, **42**:29, 1946) points out that the most common side effect of diethylstibestrol is nausea and occasionally vomiting. The nausea may cease after a few days with change in dosage or following reduction of the dose. However, if it continues, 0·65 gm. of ammonium chloride after meals and at bedtime will aid in control and thus allow continuation of diethylstibestrol therapy.

### Segmental Resection of Lung for Bronchiectasis

Polcher (*Lancet*, **1**:843, 1946) gives in the following lines the summary of his observation: Segmental resection of the lung widens the scope of surgery in extensive bronchiectasis and minimises the sacrifice of healthy lung. The operation carries no greater risk than does lobectomy. In children palpation is a useful aid to recognition of diseased segments, and for this a free pleura is an advantage. The operation has been done in 10 cases, which are briefly reported.

### Postmaturity

Wrigley (*Brit. M. J.*, **1**:619, 1946) at a meeting of the Section of Obstetrics of the Royal Society of Medicine, read a paper on the subject where he said that he had felt considerable dissatisfaction with the meaning of the word, the diagnosis and management of the condition, and the lack of teaching on the subject. Many of our difficulties were self-made, in that we acted on the assumption that if any pregnancy continued over the calculated date for its termination the fœtus would become so large as to give rise to difficulty in delivery. That this was not the case had long been recognized. Almost half the babies of 9 lb. (4·0 kg.) and over born at St. Thomas's Hospital in 1945 had been delivered before the calculated date. Another series of cases showed how often a small baby was born after the expected date. Some textbooks stated that prolonged pregnancy did not necessarily result in a large child, while others ignored the subject or stated that the child was always above the average weight and length. Textbooks were also contradictory on the diagnosis of postmaturity. The majority of authors had written on the assumption that postmaturity was synonymous with excessive develoment of the fœtus. Radiography was not of much help in diagnosis. The appearance of ossific centres varied considerably and was of little value in assessing the maturity of the fœtus. Many writers gave no advice on the management of women who had passed the expected date of confinement; some advised induction when the fœtus was postmature but did not indicate when that state was reached, while others avoided interference. Weekly examination and induction were advised when the child was large and labour overdue. Estimation of the height of the fundus would never help, especially in the last weeks of pregnancy. Girth measurement varied in different women and did not greatly increase when the fœtus was postmature, because there was no corresponding increase in the amount of liquor amnii. The following, Mr. Wrigley said, were additional physical signs of postmaturity: (1) When the fœtus was truly postmature it was large, its weight being well above 7 lb. (3·1 kg); this could be appreciated by repeated clinical examinations. (2) Concurrent with the increase in size was increase in strength and tone, which resulted in the whole fœtus becoming more rigid; this rigidity could be recognized on clinical examination. (3) The amount of liquor did not appear to increase in the last weeks of pregnancy, and therefore as pregnancy advanced the fœtus became more easy to palpate. Thus there might be a large rigid fœtus easily felt in a uterus that contained little liquor, perhaps so little that the uterine wall might be thought to outline the fœtal position and some of its limbs. These signs would be observed with reasonable certainty only if the doctor had watched the patient at regular intervals throughout the pregnancy and at frequent intervals in the later weeks. The amount of liquor varied in different women, but in all women there should be a relative, and as full time was reached a noticeable, apparent decrease in amount.

Mr. Wrigley held that ideas on pregnancy and its termination needed revision. The "expected date" could only be aproximate and it would probably never be possible at any time during the pregnancy to make a more accurate forecast. Three variations might occur: the expected date might come and go and labour start some days or weeks later with the delivery of a large postmature baby, or with the delivery of a normal-size baby or even a small baby, or, at about the calculated date, a large oversized baby would be delivered that showed every characteristic attributed to postmaturity. An apt simile was that the pregnant uterus should be regarded as an oven, and just as there were slow ovens and quick ovens so would there be a variation in the time expected in the production of a cooked joint or a mature fœtus. As a result of the differing advice in the textbooks doctors adopted one of two courses: either every woman who had passed the expected date received a medical induction or she was "left to Nature"; in the latter case the patient occasionally delivered herself of a large truly postmature baby perhaps with great difficulty and risk to both. There was no justification whatever for advising that a week or a fortnight should elapse after the expected date and then labour should be induced. If this course was adopted a number of women would go into labour later than they should be allowed to do, or, alternatively the baby might not be mature. Another objection to routine induction was that it frequently led to repeated medical inductions. Apart from the physical upheaval of such proceedings, they were accompanied by a variable degree of anxiety which increased with each failure to bring on labour. It should be a rule that if there was justification for a medical induction there

was justification for surgical induction. Doctors should continue to give patients estimated dates for their confinement, but should cease to believe and to teach that every woman would mature in the calculated 40 weeks. There should be no instructions to terminate pregnancy as a routine at the 40th week, 41st week, 42nd week, etc. Doctors should teach that by repeated observations at regular intervals there appeared a combination of physical signs that would indicate the course of action that it might well be necessary to terminate pregnancy at the 38th week for a baby that was obviously large; and that in the absence of these physical signs interference was bad midwifery.

### Treatment of Acute Prolapse of the Uterus

A new treatment of acute prolapse of the uterus has been described in the *British Medical Journal*. It was discovered by accident. A woman aged 31 had been spontaneously delivered of her second child. As there was moderate hæmorrhage, Crede's expression of the placenta was performed and the uterus became completely inverted. It was at once replaced in the vagina, but further manipulation was considered inadvisable because of shock. An obstetric surgeon, Mr. J. V. O'Sulivan, saw her seventy minutes after the inversion. She was pale and sweating, with a blood pressure of 80/50 and a pulse rate of 140. On separation of the labia the fundus of the uterus could be seen with the placenta. The treatment of shock included 3 pints of blood. Three hours later the patient had improved greatly and replacement by taxis was attempted with ether anæsthesia. This caused rapid deterioration of her condition, so a douche was given preparatory to a later attempt. When the douche was given the tip of the nozzle, guarded by the fingers, was passed toward the posterior fornix. The surgeon's forearm blocked the vaginal orifice, the vagina ballooned out and the uterus promptly returned to its correct position. The signs of shock rapidly disappeared, and uninterrupted recovery followed.

In a second case inversion of the uterus took place in the third stage of labour, and two large tears occurred in an attempt to strip off the placenta. The patient's condition became desperate, with a blood pressure of 70/40. O'Sullivan saw her nine hours after inversion, when she had improved sufficiently to warrant further treatment. Under light open ether anæsthesia the uterus was gently delivered through the vagina and the adjacent peritoneal cavity was inspected through the tears. The oviducts and ovaries were found normal. The two tears were repaired. Gentle taxis failed to replace the uterus. In spite of the ruptured uterus, which had been sutured, it was decided to attempt to replace it by hydraulic pressure. The vagina was distended to capacity by a dettol and proflavine douche, which was retained by blocking the outlet with the forearm aided by the assistant's hands. The position of the uterus was corrected, the douche can being held 2 to 3 feet above the vagina. Complete recovery followed.

O'Sulivan recommends immediate replacement of the uterus as soon as inversion occurs, before shock develops, without attempting to remove the placenta. If the patient is in shock, clean the uterus and change the complete inversion to an incomplete by gently replacing it in the vagina, then raise the foot of the bed, place a sterile pad on the vulva and treat for shock. When shock is controlled replace the uterus by hydraulic pressure, as described. Other obstetricians have reported cases in wihch hydraulic pressure was successful. —*J.A.M.A.*

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(*Concluded from page 99*)

tions (beading, rachitic rosary) and bulging forehead (cranial bosses) which respond to treatment are found in infancy and in the rare example of late rickets.

### Stigmas Suggesting Deficiency of Vitamin K

*A tendency to bleeding:*

Particularly from minor wounds, related to abnormal lengthening of the prothrombin time, developing spontaneously in newborn infants; observed in adults after treatment with dicumarol or large doses of salicylates; in advanced disease of the liver with poor excretion of bile, and in disease of the intestine, such as sprue in which vitamin absorption is disturbed.

### Treatment of Vitamin K Deficiency

*In adults:*

1 mg. of vitamin K two to three times daily with or without bile (1 gm. of desiccated bile or bile salts.)

*In newborn babies:*

1 mg. of synthetic vitamin K intramuscularly daily in oil solution for several days.

### Deficiency Symptoms

A diagnosis of vitamin deficiency only rarely can be based on symptoms or less significant abnormailities than those which have been listed thus far. However, such symptoms and abnormalities frequently accompany the more specific lesions of deficiency.

Symptoms commonly observed with deficiency of thiamine, also less conspicuously in deficiency of other vitamins, include apathy, lethargy, increased emotional irritability, hypersensitivity to noise and painful stimuli, headache, vague fears, confusion of thought, uncertainty of memory, asthenia, loss of manual dexterity, insomnia, heart consciousness, paresthesia, anorexia, nausea, flatulence, epigastric pain, constipation.

Photophobia, burning of the eyes, lacrimation and eyestrain not relieved by glasses are encountered in deficiency of riboflavin.

Other abnormalities unrelated to deficiency of any single vitamin but commonly observed in persons who are malnourished are dry, brittle, lack-luster, rebellious, so-called staring head hair, a loss of sleekness analogous to the rough coat of malnourished animals, blepharitis, spider-like telangiectasis of the face, seborrhea of the face, patchy pigmentation of the face, especially suborbital and circumoral, sinus arrhythmia, bradycardia, tachycardia, low blood pressure, loss of tone of muscles and anemia.—*J.A.M.A.*, **131**:666, 1946.

## NOTES AND NEWS

### HEALTH MINISTERS' CONFERENCE AT NEW DELHI

Inaugurating the Health Ministers' Conference at New Delhi in October last, Pandit Jawaharlal Nehru, Vice-President of the Interim Government, stressed that health was a basic problem which formed the foundation of a nation's edifice and if the foundation was weak, the building was likely to collapse.

Pandit Nehru said that various questions faced the country, some of which were controversial. But others were basic problems, health being one of them. The political and other matters might brook some delay, but problems like health which, if not given proper attention to, in time, could not be rectified. Hitherto not much attention had been paid by the State to problems like health and education. Lack of funds was the explanation. If funds could be available for big wars, there was no reason why they should not be provided for to fight against ill-health, which was like the enemy from within and weakened the nation. No doubt, it was a gigantic task, but it was one of those urgent questions which had got to be attended to if we were to avoid situations like the aftermath of the Bengal famine. So far attention had been paid more to the towns, whereas India lived in the villages. The producer of the country's wealth should be physically strong and expenditure on him should not be grudged. It is necessary to concentrate on the preventive health measures rather than on huge buildings for hospitals. Proceeding, Pandit Nehru said that there was no intention on the part of the Centre to compel the provinces to adopt a particular policy. They were free to chalk out their own measures but in matters like health co-operation of the provinces and the Centre was essential. In fact, it was really a matter of international co-operation: for with modern transport, there was always a danger of disease spreading from one part of the world to another. Inside the country itself, if one part was in a bad state, it affected the other parts as well. Pandit Nehru hoped that the mutual discussions which the health ministers were going to have on health problems would prove beneficial to the country.

Sir Shafaat Ahmed Khan, Health Member in the Interim Government gave the assurance that while detailed plans for health development were to be made and carried out by Provincial Governments, "the Interim Government will do all in their power to assist sound health development in India."

The Central Government, he said, proposed to implement the Bhore Committee's recommendations by setting up a committee to advise the Government regarding the establishment of an all-India institute for training and research, providing facilities at Calcutta for licentiates from all parts of India to take their M.B.B.S. degree and sending selected students abroad for training. A nursing college has been opened which would provide a course for a university degree in nursing. The Malaria Institute of India would be expanded. Legislation for pharmacy, dental and nursing profession would be undertaken.

Sir Shafaat announced that the Government proposed to develop health advice and information services.

A bureau was being set up to collect information regarding the equipment of medical institutions and the question of collecting population and vital statistics was engaging the Government's attention.

The survey of health conditions in the country by the Bhore Committee shows, the Health Member observed, "how serious the position is and how rudimentary and inadequate our services are" and "health, like education, must become a function of the State." The State must create the conditions for healthy living and provide as complete a health service as possible.

The Committee had rightly laid emphasis, he added, on the influence of conditions of living and environment on the health of the individual and the community; thus the responsibilities of those concerned with the health of the people extended far beyond the hospitals and "it is necessary that we should take an interest in all those Government or social activities which promote health or might be used to promote it."

Referring to the need for improvement of environmental hygiene and preventive measures stressed by the Committee, Sir Shafaat said, "even in some of the largest towns the sanitary organisation is notoriously inefficient, while in the rural areas there has been in most provinces no systematic attempt to improve sanitary conditions. If there is a question of priorities—and planning means priorities I think all will agree that an active programme for the improvement of water supply and sanitation in our towns and villages is one of the the most urgent of our needs. In regard to preventive medicines he said that science had placed within our reach powerful insecticides and drugs to fight diseases like Malaria, the direct or indirect cause of tremendous mortality, and the means for effective application of the knowledge made available, had to be found. A committee of experts had been set up to recommend what measures should be taken to avoid creating conditions favourable to the spread of malaria and its report was awaited.

Sir Shafaat emphasized the need for more vigorous measures to check epidemics in the early stages and to provide treatment for those who had the misfortune to be attacked.

Regarding the provision of health services in the rural areas, the Health Member agreed with the Bhore Committee that it was only the outermost fringe of such public services and amenities as the country enjoyed that occasionally came within the orbit of the cultivator's daily life, and said that "the time has come for an effective programme to bring these benefits of modern medical science within the reach of the cultivator. He endorsed the committee's proposal for the development of a district health organisation with a primary health centre for every 40,000 people, a thirty-bed hospital for every 2,00,000 and a secondary centre with a two-hundred bed hospital for each district.

The training of personnel, in the Health Member's opinion, was a matter which should be given special attention in the early years of development. Other matters which required consideration were results in other countries, maternity and child welfare services, industrial health services and health insurance.

Expressing his views on the question of expenditure, Sir Shafaat said: "I have no doubt that if we are serious in our desire to build up the peoples' health and do not pay mere lip service to an ideal we must devote a large part of our resources to health."

The Health Ministers from seven Provinces and a number of States attended the Conference.

The Health Ministers' Conference unanimously adopted the following resolutions:—

"The Conference endorses the objectives proposed by the Bhore Committee as objectives to be kept in view in formulating plans for a national health service."

Among the objectives suggested by the Bhore Committee are: that there should be adequate provision for the medical care of the individual in the curative and preventive fields, that special provision will be necessary for certain sections of the population, *e.g.*, mothers, children, the mentally deficient, and that no individual should fail to secure adequate medical care because of his inability to pay."

The abolition of the civil branch of the Indian Medical Service and adequate provision for research in and the application of scientific methods for the investigation of the indigenous system of medicine formed the subject matter of two resolutions adopted by the Health Ministers' Conference which concluded its deliberations on the 12th October last.

The resolution on the abolition of the civil branch of the IMS reads: "This conference of Health Ministers is of opinion that there should be no civil branch of the I.M.S. and requests that the Central Government may arrange to take back immediately the I.M.S. personnel in civil employ in the provinces, and post them on the military side to which they rightly belong."

The conference resolved that in accordance with the recommendations of the National Planning Committee, adequate provision should be made at the Centre and the provinces for research in and the application of the scientific methods for the investigation of the indigenous systems like Ayurveda and Unani with reference to maintenance of health and prevention and cure of disease: for starting schools and colleges for training for diploma and degree courses in indigenous systems of medicine; and for post-graduate courses in Indian medicine for graduates in Western medicine.

The Conference further resolved "to absorb the practitioners of the Ayurvedic and Unani systems of medicine into the State health organization by giving them further scientific training wherever necessary as health personnel, doctors, physical training experts (ustads), sanitary staff, masseurs, nurses, midwives, etc.

In all seven resolutions were adopted at the session dealing with various health matters. The conference accepted the principle of amalgamation of Medical and Public Health Departments and considered that the amalgamation should take place when a suitable opportunity occurred.

The Ministers from Madras and Bombay dissented from this view, while the Minister from Madras considered that co-ordination between the two departments was preferable to amalgamation.

The conference urged that a vigorous drive against malaria should receive priority in development programmes and that subject to adaptation to suit local conditions, an anti-malaria organization should follow the general framework of the organization proposed by the Bhore Committee. Subject to review from time to time, it was agreed that quinine production should be continued and developed up to about 2,00,000 lbs. a year.

It was agreed that boards of health and councils of experts should be constituted both at the Centre and in the provinces. It was also resolved that an active programme for the improvement of water supply and sanitation in both urban and rural areas should be undertaken.

Winding up the proceedings, Sir Shafaat Ahmad Khan, Health Member assurred the provincial Health Ministers that the Central Government would help them by giving substantial grants and enabling them in every possible way to put their health plans in operation—*Calcutta Municipal Gaz.*, **45**:15, 1946.

## COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, 1947

A Commonwealth and Empire Health and Tuberculosis Conference will be held in London on July 7th., 8th. and 9th., 1947. It will attract an attendance of prominent doctors, and the programme will give opportunities for the medical and social aspects of tuberculosis to be discussed.

## THE DISCOVERY OF INSULIN

This year is the 25th anniversary of the discovery of insulin, and the Diabetic Association is arranging silver jubilee celebrations to commemorate the event. Sir Frederick Banting was killed on active service, but his co-worker, Prof. C. H. Best, F.R.S., is living.

Attempts had been made before Banting's time to separate insulin from the other secretions of the pancreas, but none had been successful. Banting believed that he could achieve the essential separation if he were given sufficient facilities for research. He found in Prof. J. J. R. McLeod, of Toronto University, a whole-hearted sympathizer. Unfortunately, the help that McLeod was able to give was limited, but Banting was supplied with animals to work upon. McLeod also turned over to Banting a young postgraduate researcher named Charles Best. The work was beset with difficulties. Often when a solution appeared in sight the final result was unsatisfactory. Funds ran low, and Banting and Best sold many of their personal possessions to keep their experiments going. Eventually success came, and in the summer of 1921 they discovered a method of extraction of insulin. The tests on animals were satisfactory, and then came the day when the extract was first used with a human being. The patient was a young diabetic dying in one of Toronto's hospitals. He regained his strength and continued to live a normal and healthy life. For their work Banting and Best were awarded the Nobel prize, and Banting was knighted. Of the partnership only Best remains. Proof McLeod died in 1935, and Banting was killed in an aeroplane crash in 1941, while flying on a Government mission.—*Brit. M. J.*, **1**:922, 1946.

## BCG VACCINATION AGAINST TUBERCULOSIS

Soon after the German occupation of Norway in April 1940 the tuberculosis experts in the Norwegian Public Health Service concluded that there was every prospect of a serious rise in the tuberculosis morbidity and mortality. Measures to counteract this anticipated rise were discussed and, in view of the favourable observations by Heimbeck, Scheel and others BCG vaccination since its introduction in 1927, it was agreed that this vaccination should be carried out on Pirquet negative persons on a large scale. In Oslo alone about 13,000 persons were thus vaccinated by the health authorities and several times this figure in the whole of Norway. Dr. G. Hertberg of the tuberculosis department of the Oslo Municipal Health Service recently presented a study of the influence of this vaccination on the tuberculosis morbidity in Oslo. With the aid of Dr. Julie Backer, chief of the Norwegian Central Bureau for Statistics, he presents a statistical calculation showing that when the annual tuberculosis mortality in Oslo for all persons up to the age of 50 is placed at 100, the corresponding figure

for BCG vaccinated persons is about 18. This comparison is even more favorable to BCG with regard to the number of infectious cases of tuberculosis, the figures being respectively 100 and 10.—*J.A.M.A.*, **131**:59, 1946.

## MEDICAL PHOTOGRAPHY

A Medical Photographers' Group has now been constituted within the Royal Photographic Society. At its inaugural meeting Surg. Rear-Admiral C.P.G. Wakeley remarked that the medical profession has hitherto had to rely largely for its records upon free-hand artists, and some excellent work has been done, but such service is often not available, and increasing resort has to be made to photography, alike in the operation theatre, the ward, the out-patient department, and the post-mortem room. Given the right technique, no more accurate method exists. Admiral Wakely spoke of the value of records made before and after treatment, operative or other, and insisted on the need for such pairs of photographs to be on the same scale and to be made so far as possible according to the same procedure. A number of speakers, including photographers attached to large hospitals and free-lance medical photographers, gave an account of their experiences, which suggested that photography now has an importance in many departments which calls for a highly trained expert. Dr. Richardson Billings described a method he has worked out for photography in the operating theatre. A usual method is to have a long-focus lens in the camera and lights fixed above the table, well out of the field of surgical activity. Dr. Billings has employed a different method. From his heavy-based tripod rises a perpendicular standard supporting baseboard so arranaged as to give universal movement and to carry the camera and lamps. The illumination comes from photoflood apparatus mounted in chosen positions around a form of lens hood, with a central incandescent lamp for focusing. The novel feature, however, is a mirror—or it may be a prism—set at an angle of 45° to the optical axis of the camera, the principle being the same as that of the laryngoscope and giving a "surgeon's eye view" of the field of operation. It is claimed that this eliminates the distortion and fore-shortening inevitable with a camera at any other angle or distance. The arrangement also fulfils two necessary conditions: that the photographer and his apparatus must keep out of the way of the surgeon, and that the apparatus must need the bare minimum of preparation. Among experiences related by photographers was the obtaining of a rapid sequence of films to illustrate the delivery of twins by Cæsarean section a task requiring unexpected mobility on the part of the photographer and his apparatus.—*Brit. M. J.*, 1:961, 1946.

## TRAINING OF GENERAL PHYSICIANS

At a comitia held on 31-1-46 ,the Royal College of Physicians of London approved the following report from its council:—

*Criteria for Consultants*—The council considered the criteria for consultants which had already been approved by the three Royal Colleges:

1. Consultants must have received their training at an approved hospital. Each college shall approve hospitals as suitable for training in its own branch of the profession and recognition shall be granted by the standing joint committee on the nomination of the individual college concerned.

2. Consultants shall have a minimum of five years' approved training and experience after qualification.

3. Consultants must hold an approved higher degree or diploma.

4. To be approved as a consultant, a candidate must hold or have held a recognised appointment to a hospital.

5. Consultants must not engage in general practice.

The council approved them in principle as applying to general physicians, but pointed out that training might be undertaken at more than one hospital. They also agreed that the consultant should have a minimum of five years' approved training and experience after qualification. This should be held to mean five years after registration. The council agreed that the M.R.C.P. examination should continue to be a test of the candidate's knowledge of general medicine. It was thought that it should not be taken earlier than one year after registration.

*Training of Physicians in General Medicine*—The council agreed that it was essential that the required training for general physicians should be as elastic as possible within the general framework already agreed upon. They agreed that the following minima should be expected:

1. Candidates should hold a resident appointment in an approved general hospital for at least one year after registration. During six months of this period, the post held should be that of house-physician. The remaining six months should be spent in another junior medical appointment such as house-surgeon, house-physician in a special hospital, or resident in one of the special departments.

2. Candidates should hold a clinical appointment such as that of a registrar or chief assistant for at least two years in an approved general hospital. During this time, he should be encouraged to undertake research work or to hold some additional appointment such as a demonstratorship in a department of physiology, anatomy, pathology, or biochemistry.

3. Candidates should spend at least one year in research or travel or in some non-clinical subject, such as physiology, anatomy, pathology, or biochemistry.

4. No rigid requirements should be laid down for the remaining period of training. A general physician should have some knowledge of the work of special hospitals such as sanatoria, children's hospitals, mental hospitals, &c., and appointments in such hospitals should be recognised. A period of six months spent in general practice might be allowed to count as part of the five years training.

The council agreed that there should be no rigid order for holding these appointments, and they emphasised that the times suggested were minimal and not maximal—*Lancet*, 1:208, 1946.

## REVOLT FROM THE BEDPAN

The designer of the bedpan is presumably long dead. Two things, however, are certain: he had never been a patient and had never met a nurse. His pan has one virtue—thanks to its flat bottom and inward-curving brim it does not easily upset in the bed—but as Dr. Douglas McClean points out (*Lancet*, 1:834, 1946) everything else is wrong with it. It is too shallow

to contain deodorant; the feeble, the elderly, and the surgical case have to be helped on and off it at the cost of great physical exertion; the weak cannot balance on it, the constipated cannot bear down; the whole ward is offended by the smell; and the patient with a bulky stool endures the sensation described by soldiers as being "Jacked off the pan." A not uncommon way to die is from cardiac syncope or pulmonary embolism while on the bedpan.

These drawbacks alone should be enough to condemn it, but in addition a series of objectionable practices surrounds its cleansing. Sluice-rooms, in most British hospitals to-day, are small and primitive and methods of washing pans offend against the hygiene standards not only of a hospital but even of the ordinary household. What local authority would countenance lavatory pans which splashed the housewife with dilute fæces? What woman who had later to handle food would care to dip her hands in fæcally contaminated water? The junior nurse often has to accept both experiences. In too many hospitals she brings the soiled pan, covered by a cloth, through the ward and inverts it over a sink fitted with a small spray or jet intended to flush it; the pan is thus rinsed in dilute fæces, and the nurse receives her share of splashes. Rubber gloves are a thing of the future; dipping her hands into the sink, she graps the contaminated pan and finishes washing it with a mop, taken from a weak solution of lysol, and used repeatedly. After a final rinsing, the pan is left inverted on the draining board —often a wooden one which connot be properly cleahed or sterilised. The smell from the sink is permanent; the clatter of the pans can be heard in the ward; the nurse washes her hands hurriedly and goes off to the next job—to move or lift patients, to make beds, or cut bread-and-butter. The bedpan is not sterilised before it is given out again; it is not reserved for any one patient; usually bedpans are too scarce to make this precaution possible. Pans are "sterilised" once a day, in the morning, by rinsing in lysol and water; and if the sluice-room is small this rite may be carried out in the patients bathroom. Urine bottles are rinsed in a similar manner, and the dangers of such a haphazard practice in a general ward need not be detailed. In maternity wards some attempt at hygiene is customary—bedpans are marked or numbered, and a steriliser is provided—but flushing arrangements are often of the crude type described. What follows from these old customs? First, any infective bowel organism is liable to be distributed round the ward either by the pans themselves or by the hands and clothing of the nurse; secondly, student nurses who will not tolerate such dirty practices, and possible recruits who revolt from the mere account of them, are lost to nursing. Those who think the disposal of excreta in hospital an unimportant detail should bear these facts in mind.

What alternative methods offer? Good sluicerooms have been designed and installed in some hospitals; yet there are modern hospitals erected just before the war which has the old ineffectual equipment. In the United States, Canada, South Africa, and a few British hospitals the tipper system is in use. The nurse presses pedal with her foot, a flap in the wall drops open, she puts the bedpan in, closes the flap, turns a handle, and the pan is flushed with water and sterilised with steam. Some such system must of course become universal, but in the present state of the building industry many years will pass before all our hospitals are so equipped. Short term measures must be less revolutionary. Clearly there should be enough bedpans in a ward for every patient to have one marked with his name or bed number. Enamel pans, whose chipped and cratered surfaces harbour organisms, should be scrapped in favour of pans made of aluminium or other light metal. These should be designed by anatomists. The Anatomy Department at Oxford was successful in designing a chair for a ship's gunner directing fire at an approaching aircraft: here is an equally difficult but more universal problem which needs solving at once. Besides being easy to clean, the pan should be easy to slip under the helpless patient and so shaped that he is comfortable and able to use the necessary muscles during defæcation. The pan could be lightly filmed with an appropriate deodorant.

Such measures will reduce the objections, but not abolish them. The aim should be to make the use of a bedpan an occasional rather than a routine ordeal. Dr. McClean makes the thoroughly practical suggestion that light metal-framed commodes with movable receptacle could be brought to the bedside. Few surgical patients need complete rest in bed for more than a few days, and many medical patients are up daily; even for the patient with coronary thrombosis moving on to a commode would surely be less risky than wriggling and straining on the bedpan. Paraplegic patients, if able to sit up, find a commode specially helpful, since the action of gravity helps the paretic bowel. The commode receptacle should be made of light metal and should be deep enough to hold some deodorant fluid, which would simplify cleaning besides keeping the ward pleasant. All bedpans and commode receptacles should be boiled immediately after cleansing, and all sluice-rooms should contain a steriliser for this purpose; even a zinc bath on a gasring is better than nothing. Wooden fittings in sluice-rooms should be removed without delay, and the sterilised pans should be placed in a metal rack till needed. These racks might carry hot pipes, so that the pans are always warmed and ready; at present nurses warm them with hot water before giving them out. Another plan would be to distribute pans from a heated trolley. They should certainly be collected on a trolley with shelves and doors; there can be no good reason why patients should have to watch nurses ringing through the ward, pan in hand, or why the nurse should have to make twenty journeys to the sluice when one would suffice. The cleansing of pans without proper equipment presents a much more serious problem—an example of the need for nursing research. Scientifically minded matrons and sisters, in collaboration with surgeons and bacteriologists, must devise a non-touch technique which can be taught to junior nurses. Properly taught this should give the student nurse an insight into aseptic technique which will stand her in good stead throughout her training, besides turning a nauseating job into a piece of technical virtuosity. We should welcome suggestion. —*Lancet*, 1:520, 1946).

## I. M. A. DISTRESS RELIEF FUND

The following further donations to the Indian Medical Association, Distress Relief Fund, are gratefully acknowledged:

Shikarpur Branch: Dr. Kishinchand Bulchandani Rs. 51|-; Dr. Govindram D. Punjabi Rs. 11|-; Dr. Java L. G. Rs. 11|-; Dr. Himathram P. Khatri Rs. 10|-; Dr. Chaturbhuj N. Pherwani Rs. 5|-; Dr. Tarachand R. Lalla Rs. 5|- and Dr. H. S. Paryani Rs. 5|- Total Rs. 98|-. Dr. Sudhir Nath Sen, B.SC., M.B., Lalkothi, Jamalpur P.O., Monghyr Rs. 100|-. Capt. K. L. Saha, M.B., Chapra Rs. 20|-. Messrs. T. M. Thakore & Co., Bombay Rs. 101|-. Saugor Branch Rs. 51|-. Ratlam Branch Rs. 50|-.